IMPERIAL MYCOLOGICAL INSTITUTE 10 SEP 1944

TROPICAL DISEASES BULLETIN

VOL. 41.] 1944. [No. 6.

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Issued under
the Direction of the
Honorary Managing Committee of the
BUREAU OF HYGIENE AND TROPICAL DISEASES,
Keppel Street, London, W.C.1.
(Telephone: MUSEUM 3041)

[Price 2/6 Net. *Entered as Second Class Matter in the U.S.A. Post.* [Annual Subscription 21/-

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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 41.] 1944. [No. 6.

THE GEOGRAPHICAL DISTRIBUTION OF MITE-BORNE TYPHUS FEVER.

[TSUTSUGAMUSHI DISEASE ; JAPANESE RIVER FEVER ; SCRUB TYPHUS ; MITE FEVER.]

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[The name mite-borne typhus is applied, in this study, to the rickettsial disease which has been known by the names quoted in the heading of this paper, and other names. The researches of LEWTHWAITE and SAVOOR (1940) indicate that there are no essential differences between the diseases to which these names have been applied, and that finding has been accepted by the Bureau of Hygiene and Tropical Diseases. MEGAW's view (ROGERS & MEGAW, *Tropical Medicine*, 1942, p. 176) that this disease should be included in the typhus group on grounds of aetiology is also accepted. It seems unnecessary to create a division in the rickettsial diseases when the aetiological agents are so much alike and the modes of transmission so similar.]

Mite-borne typhus fever is known to occur in the following countries : Japan, Formosa and the Pescadores Islands, Borneo, New Guinea, Queensland, Java, Sumatra, Malaya, French Indo-China, Burma, India and Ceylon. Various authors have stated that it occurs (or probably occurs) in Korea, Shanghai and other places in China, and in the Philippine Islands, but the opinions appear to have little evidence to support them.

As the name tropical typhus has been used to include both murine typhus and mite-borne typhus the diagnosis is doubtful where agglutination tests have not been made.

With regard to arthropod vectors the fact that they have been found on an animal does not necessarily mean that they are ectoparasites of that animal ; their presence might be accidental and temporary.

Japan.

The disease appears to be limited to areas near the banks of certain rivers on the west side of the main island (Honshu, Hondo or Nippon); it is endemic in the Niigata province in this island. The following areas are mentioned:—

Akita province—rivers Omono, Minase, Nishimanai, Masuda and Inaba.
Yama province—river Mogami.
Niigata province—rivers Shinano and Aka.

Districts of certain rivers:—

Uonuma river—Minami-Uonuma district.
Shinano river—Koshi, Santo, Minami-Kambara, Nishi-Kambara, Naka-Kambara.
Aka river—Kita-Kambara.

The disease is transmitted by *Trombicula akamushi*, which infests the field vole, *Microtus montebelloi*, other rodents and some birds.

Formosa.

The population is 5,200,000. The island is divided into five prefectures and three Districts. In the western part of the island there are five prefectural governments, *viz.*, in Taihoku, Shinchiku, Taichu, Tainan and Takao; the eastern part is sparsely populated and is divided into two districts, Taito and Karenko. The Pescadores (Bôko) Islands form another district.

In the main island the disease is very widely distributed (contrary to what occurs in Japan), being found in all five prefectures and two districts. It is found not only near river banks but also in cultivated fields, foot-hills, jungles in the plains and in the mountains, which rise to a height of 6,500 feet; it is, however, mostly seen in valleys and foot-hills. It is most prevalent in the eastern part of the island (Karenko and Taito), is fairly prevalent in the plains and foot-hills of Takao prefecture in the south, and occurs also in the central mountains in Taman, Taichu and Shinchiku and in the river basin of Taihoku prefecture.

While in Japan the disease is limited to the period May to October, it occurs all the year round in Formosa but is most prevalent from May to December, the peak period being from July to October.

It is transmitted in Formosa by *Trombicula akamushi*. The larvae are found on: *Rattus rattus rattus*, *R. rattus rufescens*, *R. norvegicus*, *R. losea*, *R. coxinga*, *Apodemus semotus*, *A. agrarius*, *Mus musculus* and *Mus formosanus*; also on *Crocidura murina* (the shrew) and on the dog, ox, buffalo, and some birds—fowl, pheasant, *Turnix taigour* (button quail) and *Centropus javanicus* (crow-pheasant). In the endemic area *R. losea* and *A. agrarius* are commonest and are heavily infested. A strain of rickettsia was isolated by the author of the paper in which this information is given (Kaoru MORISHITA) from *R. losea* captured in the endemic area.

In 1935–1938 there were 18, 26, 16 and 22 cases with 0, 2, 4 and 6 deaths respectively.

The following localities are mentioned by Jura HATORI (1919) :—

(*a*) Karenko district.
  (1) Mokkui and Rokei valley.
  (2) Yoshimo plantation.
  (3) Kotobukimura and western Tayoda plantation.
  (4) Hayashida plantation, Horin-Sho and neighbouring forests.
  (5) Maribashi plantation.
  (6) Seisu valley.
  (7) Shinjo and Takkiri valley.
(*b*) Giran district.
  Dainanwo river valley.
(*c*) Toyen district.
  Mount Kappan (1 case).
(*d*) Schinchiku district.
  Shakaro village (1 case).
(*e*) Kagi district.
  Forest of Mount Ari.
  Tappan village.
(*f*) Ako district.
  Airyo valley
  Maruyama near Shirinkaku, Koshen.
  Plains between Ako and Chosha.

Pescadores (Bôko) Islands.

These comprise 63 islands in Formosa Strait.

The houses are surrounded by the endemic area and therefore all the inhabitants are exposed to infection. Tsutsugamushi disease is not known to be contracted in the fields far from human dwellings; this may be because a strong monsoon carries salt water and damages grasses and plants, so producing unfavourable living conditions for *Trombicula akamushi*. The ground around the dwellings is protected by coral walls and the trombicula develops there. The trombicula develops in the ground inside the coral walls.

Rattus rattus rufescens [the common house rat in Formosa and the Pescadores Islands] was found heavily infested with the mites and rickettsiae were found in its tissues.

The season is from April to November only, with a peak in June and July. Children are especially affected, 70 per cent. of cases being in children under 15 years of age, and 38·6 per cent. in those under 5 years. There are 30–80 cases a year; the case mortality varies up to 21 per cent.

Borneo.

A fatal case of mite fever in a European was reported by BESSEM in 1935. The infection was acquired in the western Division of the island. The diagnosis was confirmed serologically, the serum agglutinating *Proteus OXK* to a titre of 1/1500 and being negative with *OX19*. A case of " tropical typhus " was reported from Brunei, in the north of the island, in 1939.

New Guinea.

The disease occurs in the Mandated Territory of New Guinea, including New Britain, and in Papua. Although DE ROOK reported in 1938

that endemic typhus (" pseudotyphus of Schüffner ") did not occur in Dutch New Guinea, GUNTHER saw a fatal case which had been contracted within a very few miles of the border of Dutch New Guinea. In the Mandated Territory it appears to affect the white races only, the natives being apparently immune [but see Papua, below].

Gunther gives the following distribution of cases :—

	Cases		Cases
Morobe District—		Madang District—	
Wau area	47	Madang area... ...	2
Upper Watut area ...	5	Karkar Island ...	1
Bulolo-Bulwa area ...	4	Sepik District—	
Ramu area	1	Green River area ...	1
New Britain	2	Maprik area ...	2
		Aitape area	1
		Wewak area... ...	1

Clinically and serologically the fever resembles tsutsugamushi disease. The vector, according to Gunther, is probably *Trombicula minor*. Its principal hosts are : Bandicoot (*Echymipera cockerelli*) ; bush pig (*Sus papuensis*) ; bush fowl (*Megapodius duperreyi*) ; bush turkey (*Talegallus jobiensis*) ; cassowary (*Casuarius casuarius*) ; ground pigeon (*Gallicolumba jobiensis*).

Papua.

GUNTHER says that according to Dr. F. J. WILLIAMS, Chief Medical Officer, no endemic typhus has been observed in white people, but several cases of a similar form of fever have recently been found among natives. Gunther remarks that the Papuans are a different race from the natives of the Mandated Territory and, unlike the latter, suffer severely from the bites of mites.

LUPSON (Port Moresby) quoted by Gunther, says that " scrub itch " in the Delta Division is caused by a mite resembling *Trombicula hirsti*. Though natural barriers may prevent spread of the disease to Papua, Gunther thinks that it may spread along the coastal districts into the neighbouring territories.

MAY (1941) reports two cases in Europeans in Papua. He thinks it probable that the disease has long existed there in the natives, though this is the first occasion on which its presence has been proved by serological tests.

PARK and OFFENKRANTZ (1943) record 36 cases of mite-borne typhus diagnosed clinically and serologically, in the " South Pacific area."

Queensland, Australia.

There has been some confusion owing to the occurrence in north Queensland of several fevers with similar clinical characters. They have been called by various names :—Mossman fever, scrub fever, endemic glandular fever, Sarina or West Plane Creek fever, coastal fever. These were investigated by HEASLIP, MATHEW and others.

According to Heaslip dengue and leptospirosis also occur. The coastal fevers include tsutsugamushi and another fever caused by an organism related to the anthrax bacillus ; both infections may occur

together in the same patient. Tsutsugamushi was definitely diagnosed by serum agglutination of *Proteus XK* in 1935. It occurs in the eastern coastal area of north Queensland between Cooktown and Ingham. Heaslip gives the following localities :—West Cairns, Double Island, Babindo, Tully, Edmonton, Mourilyan, El Arish, Jordan Creek, Cairns Intake, Little Mulgrave, Gordonvale, Queerah, Redlynch, Mossman, Daintree, Edgehill, Cooktown, Ingham, Meerawa, Yorkies' Knob.

Most of his patients lived in the Cairns district. He thinks that the disease probably occurs in other places in Northern Australia.

MATHEW (1938) mentions also : Innisfail, Tully, Kuranda, Tolga, Atherton and Millaa Millaa and says that in the Cairns area there are at least four clearly defined foci of *XK* fever—West Cairns and Edgehill; Edmonton and Hambledon ; Intake and Redlynch ; Double Island and Yorkies' Knob.

Tsutsugamushi occurs mostly among cane-farm workers and road makers clearing the scrub. The probable vector is *Trombicula deliensis*. The serum of one bandicoot (*Perameles nasuta*) agglutinated *Proteus XK* 1/250.

Java.

Cases of mite fever are said to be rare. WOLFF and DE GRAAF (1939) reported two cases contracted in scrub jungle. Serum agglutinated *Proteus OXK* 1/200 and 1/400, and numerous rickettsiae were found in guineapigs inoculated with the patients' blood.

LEIMENA (1941) described a case in a man from Bandoeng who had never been out of Java. The Weil-Felix reaction with *Proteus OXK* was positive at a titre of 1/400.

Sumatra.

Mite fever occurs on the east coast of Sumatra and especially in Atjeh at the northern extremity. VAN DER SCHROEFF (1941) reported an epidemic in the Atjeh area among coolies clearing jungle growth. *Trombicula deliensis* and *Amblyomma* are abundant and parasitic on mice, rats and the lalang bird. The local name of the fever, according to KOTTER (1940) is " Seulimeum fever " ; he mentions the localities Koetarodja and Seulimeum. WALCH (1922) found the incidence chiefly among workers on tobacco estates situated between the central mountain chain and the east coast ; the tobacco fields are only cultivated for one year in eight or nine years. Mite fever was also found in workers on overgrown rubber estates.

Malaya.

The disease is known to occur in the four Federated Malay States—Selangor, Pahang, Perak and Negri-Sembilan and, according to ANIGSTEIN (1933), six cases were reported from Kedah. It occurs sporadically. Cases of tropical typhus, some of which have been confirmed serologically with *Proteus XK*, have been reported also from Johore, Kelantan, Trengganu, and the Straits Settlements.

The insect vector is thought to be *Trombicula deliensis* and the animal reservoir is probably the Malayan rural rat, *Rattus rattus jalorensis* ; GATER found *Trombicula akamushi* on estate labourers in Selangor and also on *Rattus rattus diardi*, the common urban rat, and *R. rattus jalorensis*. He found *T. deliensis* frequently infesting these rats and

also other rats, squirrels and some other animals, but less commonly on man than *T. akamushi*. LEWTHWAITE found that most of the 154 cases of rural typhus observed during the period 1927–1930 occurred in outdoor labourers engaged in pruning and weeding on a palm oil estate; some cases occurred in similar workers on rubber estates. O'CONNOR treated the disease in bullock drivers and cowherds who visited overgrown abandoned agricultural land. There is no clear seasonal influence in Malaya, but the seasons are ill-defined there.

French Indo-China.

Fever of the tsutsugamushi type occurs in the five divisions—Cambodia, Cochin-China, Annam, Laos and Tonking. Neither vectors nor animal reservoirs have been determined.

Burma.

MAITRA and GUPTA (1936) made extensive serological tests. They could not state precisely where infection occurred but gave the following localities from which positive *XK* sera were received.

Lower Burma—Rangoon, Syriam, Henzada, Prome, Toungoo, Bassein.

Upper Burma—Yametha, Meiktila, Kyauksi, Shiwebo, Chin Hills, Katha, Southern Shan States, Northern Shan States, Mandalay, Maymyo, Myitkyima.

India.

The mite-borne type of typhus fever has been found in the Simla Hills, Madras and Bombay. WOODHEAD and DUTTA (1941) examined sera from various parts of Assam where no typhus fever has hitherto been reported. They used *Proteus OX19*, *OXK* and *OX2* and found that 8 out of 203 sera gave diagnostic titres with *OXK*, one agglutinated at 1/3,500, another at 1/800 and a third at 1/550.

BOYD (1935) found 43 cases whose sera gave preponderating agglutination with *Proteus XK*; of these 35 were clearly defined, 21 being British and 14 Indian. He mentions the following localities :—

Districts—Lahore (15 cases), Meerut (5), Bengal and Assam (6), Deccan (8), Burma (1).

Stations—

British—Kasauli, Calcutta, Dagshai, Sabathu, Chakrata, Dinafore, Jhansi, Mingaladon.

Indian—Bareilly, Alipore, Jubbulpore, Trimulgherry, Landsdowne.

There was no evidence of mite-transmission.

BUSH (1936) recorded six cases, four British and two Indian. He gives the following localities in the Simla Hills :—Solon, Dagshai, Kasauli, Nalwa (near Kasauli).

MACNAMARA (1935) described an epidemic in the Simla Hills Stations —Sabathu, Dagshai and Kasauli. No vector or reservoir was found.

At the King Institute, Guindy, Madras Presidency, out of 4,381 sera examined, 16 gave a positive result with *Proteus OXK* at a titre

of 1/200 or more. No virus was isolated. In the 1936 report the sera of 66 out of 134 squirrels examined were positive to *OXK* in dilutions of 1/25 to 1/200.

Bombay.

PATEL (1943) found that the serum of one out of six cases of typhus fever was positive to *OXK* at 1/1500 dilution.

Ceylon.

Lucius NICHOLLS (1941) reported a case in a European who apparently contracted the disease while on a shooting trip in the east of the island. His serum agglutinated *Proteus OXK* to a titre of 1/500.

WIJERAMA (1936) observed two cases, one in an Indian and the other in a Sinhalese. Both gave agglutination with *Proteus OXK* 1/5000, and rickettsiae were found in guineapigs inoculated with the blood of one patient.

China.

Japanese authors state that fevers like tsutsugamushi are described in old Chinese writings, but it is at present not known to occur in China.

RAYNAL (1939) in a paper on exanthematic fevers in Shanghai, states that there certainly exist locally other exanthematic fevers which resemble Japanese river fever, but their presence has not yet been convincingly demonstrated.

Korea.

WEIR (1915) described 15 cases of fever which he called "paratyphus," occurring in the spring and early summer.

DE LANGEN and LICHTENSTEIN (1936), referring to mite-borne typhus, say that what is in all probability the same disease is also found in Korea and the Philippine Islands.

Philippine Islands.

The only evidence of the possible existence of fevers resembling mite-borne typhus appears to be the report by ASHBURN and CRAIG in 1908 of two cases seen there in 1906 by the former. No further cases are recorded in the *Philippine Journal of Science* since that date. Several text books (MENSE, STITT, MANSON-BAHR) state that it occurs or probably occurs there, but these authors may be relying on the report of Ashburn and Craig.

Samoa.

POLECK (1925) reported the presence of a fever clinically resembling typhoid fever but giving negative results with agglutination tests. He suggested that it was probably "pseudotyphus." There were some cases in Europeans.

Other Places.

Although mite-borne typhus does not appear to have been reported from Siam, Hainan, and other Pacific islands, it cannot be assumed that they are free from it.

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SUMMARY OF RECENT ABSTRACTS.*

V. LEISHMANIASIS.

Visceral.

Epidemiology.

Boix Barrios (p. 23) refers to the epidemiology of kala azar in Spain, where incidence is most heavy on the Mediterranean coast and in the Madrid area. The infantile form predominates and is characteristic of Mediterranean kala azar; the chief reservoir is the dog. Kowalzig (p. 120) refers to five cases of kala azar in German soldiers stationed in Spain during the civil war.

The formol gel reaction is positive in 81 per cent. of dogs in the Petrich district of Bulgaria; Drenowsky (p. 121) concludes from this that canine leishmaniasis is widespread there.

Potenza and Andeze (p. 891) have diagnosed, by viscerotomy, a second case of kala azar in Venezuela. Attempts to correlate the two cases with the presence of *Phlebotomus* have not been successful, but more work is obviously needed.

Transmission.

Swaminath *et al.* (p. 227) trace the course of the various investigations made, since the early days of the Kala Azar Commission, on the transmission of the disease. *Phlebotomus argentipes* was suspected on epidemiological grounds, but experimental proof of transmission to animals and man was almost impossible until it was found that after the infecting feed the flies should be maintained on a diet of raisins instead of blood. On this diet the development of flagellates was much greater, and led to blockage of the pharynx; flies in this state were found to be capable of transmitting infection. The authors report successful transmission by the bite of such flies to all of five volunteers with incubation periods of five months and upwards. These successes may have been due to the adoption of this technique, but the virulence of the parasites may have been a factor.

Parrot *et al.* (p. 527) in Algiers caught a large number of sandflies, over a period of five months, in the kennels of dogs known to be suffering from generalized leishmaniasis. Most of the flies were *Phlebotomus perniciosus* and *P. longicuspis*, and 20 and 16 per cent. respectively were found to harbour flagellates of the leptomonas type, usually in the stomach, but occasionally in the oesophagus or proboscis. These two species are therefore to be regarded as vectors of kala azar. Investigation indicated that infection is not transmitted from adult female sandflies to their offspring.

Clinical Features.

Peláez Redondo (p. 375) notes that in Spain, as in other Mediterranean countries, there has been an increase in the incidence of kala azar in adults in recent years. He describes the clinical features,

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1943, v. 40. References to the abstracts are given under the names of the authors quoted, and the pages on which the abstracts are printed.

noting that spleen puncture is the most certain method of diagnosis. Parasites are less likely to be found by sternal puncture, and blood examination, in his patients, was invariably negative. LAFUENTE and GODARD (p. 892) describe two cases of kala azar in children in the province of Constantine, Algeria. In one the diagnosis was made by spleen puncture, in the other the leishmania were found abundantly in a film of the peripheral blood.

MIRZOIAN (p. 295) describes, from Samarkand, an early sign of kala azar in children. Several months before the disease can be diagnosed clinically there appear on the face minute papules (the size of a pin head) which increase to the size of a lentil, are pink or red in colour, and disappear in a few months, leaving pigmented spots. Leishmania can be found in these papules. Later the sternal marrow commonly becomes positive, and lymph glands and spleen enlarged. The papules do not develop into oriental sores, and as kala azar and oriental sore are only very rarely found together, the author considers that the papules are part of the kala azar syndrome. He thinks that the papules develop at the sites of sandfly bites, since they appear in summer and autumn, are found only on the face (which is most exposed) and because leishmania are not found in scrapings from the skin of other parts. The author emphasizes the value of these papules in early diagnosis.

COLE (p. 229) reports kala azar from the region north of Lake Rudolph, Abyssinia. Over half the patients admitted to hospital died, and in some of those who survived a nodular rash developed, which coalesced to form a warty mass, and in which leishmania were found. The mass finally regressed; no treatment appeared to be necessary for this condition.

CHUNG (p. 228) reports a case in which the lymphatic glands of various regions of the body apparently became infected, probably from a lesion in the mastoid area, but in which good general resistance presumably prevented visceral infection. One excised gland proved infective for a hamster, but it was not possible to find leishmania in liver or sternal puncture material or in the excised gland.

NIYOGI and RAY (p. 762) have prepared an antigen, for use in a complement fixation test, from washed flagellates of a 48-hour culture of *L. donovani*. The test was positive in 10 cases of kala azar, but not in two of cutaneous leishmaniasis or in several patients with other diseases.

Treatment.

NAPIER *et al.* (p. 121) report on the treatment of 100 cases of Indian kala azar with stilbamidine, the introduction of which, in their opinion, constitutes a great advance in therapeutics. They note that for diagnosis spleen puncture was the most reliable procedure, and that the aldehyde test was positive in 74 cases. The patients were of all ages from infancy to over 45 years. Stilbamidine was administered as a 1 per cent. solution, usually intravenously, daily for 10 to 15 days, in doses (for adults) of 0·025 gm., 0·05, 0·06, 0·075, 0·09 and 0·1 gm., up to a maximum of 1·0 mgm. per pound of body weight. Reactions are common, sometimes alarming, but apparently free from danger, and may be controlled by injections of adrenaline before the stilbamidine is given. In this series there were two deaths and two relapses; the remainder were cured.

KIRK and SATI (p. 684) report on 43 cases of kala azar treated, in the Sudan, with aromatic diamidines. Eight patients died (but five were in an advanced stage) and 35 were discharged as provisionally cured. Of these 35 patients, followed up for 2½–3 years, four could not be traced and three died. Thus 28 of 43 patients were known to be alive after a considerable lapse of time. [It will be remembered that kala azar in the Sudan is a severe disease with a high mortality rate.]

FULTON and YORKE (p. 23) discovered that stilbamidine becomes much more toxic for mice if a solution is allowed to stand in sunlight before use. Exposure for two days greatly increased toxicity, but no further increase was found after exposure for 14 days, nor had boiling or keeping in the dark for 14 days any comparable effect. The immediately fatal results produced in mice by injection of stilbamidine exposed to light are not the same as the degenerative liver changes and nerve lesions noted in man and animals; the latter seem to be caused rather by cumulative action than by acute toxicity. It is, therefore, not possible to say if the late effects in man are due to exposure of the drug to light, but the investigation does lead to the conclusion that solutions for therapeutic use should be freshly prepared. In comment HAWKING notes that a fresh solution is strongly fluorescent in ultra-violet light, but that fluorescence gradually diminishes on continued exposure; it is, therefore, clear that energy is drawn from the light and that molecular change occurs.

BARBER *et al.* (p. 376) have followed up this work. They think that the toxic product is almost certainly 4 : 4′-diamidino phenyl benzyl carbinol, and that the reaction to light which occurs in aqueous solution is an addition of the elements of water to the double bond of the stilbene linkage. Other therapeutic diamidines have shown no such biological or chemical properties, and the change is associated with the unsaturated stilbene linkage; the amidine groups are not affected. The toxic substance has been isolated and its pharmacology studied; its action differs rather quantitatively than qualitatively from that of the original substance. The toxic product is almost inactive therapeutically against *Trypanosoma equiperdum*.

Investigating this subject further, FULTON (p. 683) has shown that only the unsaturated compounds are affected. Water is added on at the unsaturated linkage, and the solution becomes more toxic and less therapeutically active. Solutions of unsaturated amidines [such as stilbamidine] should be freshly prepared for use, or should at least be stored away from light. GOODWIN (p. 684) has confirmed these findings by spectroscopic methods.

HENRY and GRINDLEY (p. 122) have studied the effect of various substances on the fluorescent property of stilbamidine. In the course of this work they noted that when solutions of stilbamidine are added slowly to normal saline, a precipitate appears which redissolves on shaking; this observation is relevant to the optimum rate for intravenous injection. The authors give details of a fluorescence test for estimation of the amount of stilbamidine in fluids; the test depends on the fact that fluorescence persists in filter paper on which a spot of the fluid has been placed. The test can be applied to serum and other body fluids, and to urine. In this way it has been shown that, after injection, excretion of the drug takes place in the urine, but ceases after about 2½ days, by which time about 10 per cent. has been eliminated. When stilbamidine is added to citrated blood, about 85 per cent. is adsorbed to the red cells, and cannot be recovered by

haemolysis or other methods. In comment HAWKING notes that if stilbamidine is adsorbed by the red cells it is probably in some non-fluorescent form, since fluorescence cannot be detected in the cells of mice injected with the drug.

WIEN (p. 682) has studied the pharmacology of certain aromatic diamidines. Poisonous doses cause general depression of the nervous system and death from respiratory failure; with repeated sublethal doses symptoms suggesting cumulative poisoning occur. The fall in blood pressure which takes place after intravenous injection is prevented or much reduced in animals by previous injection of calcium; it is due mainly to peripheral vaso-dilatation. The effects on the heart are small and transitory.

WIEN *et al.* (p. 683) show that certain of these aromatic diamidines produce hyperglycaemia, partly due to the increased output of adrenaline in the experimental animals. Chronic poisoning leads to fatty degeneration of the liver, and the compounds also act on the kidneys, which show cloudy swelling and fat globules in the convoluted tubules, with increase in blood urea and non-protein nitrogen.

CHUNG *et al.* (p. 229) in Peiping report that the results obtained with solustibosan in kala azar are as good as those with urea stibamine or neostibosan, but that in terms of antimony the amount required is much greater. The dose is 6–12 cc. on alternate days to a total of 60–162 cc. The solution contains 20 mgm. of metallic antimony per cc.; it can be given intravenously or intramuscularly.

CHUNG and CHOW (p. 229) report that the sodium salt of mannite antimonic acid, which contains 21 per cent. of antimony, gives a higher rate of cure in hamsters infected with kala azar than any other antimony compound. Solutions of 30 and 50 per cent. are used; they can be sterilized by boiling and can be injected intravenously, intramuscularly or subcutaneously. Toxicity is relatively low, and three times as much antimony can be given in this form as in the form of solustibosan.

BRAHMACHARI and BASU (p. 121) report an unusual case of dermal leishmaniasis which developed two years after apparent cure of kala azar; treatment with urea stibamine has not prevented a later relapse.

CUTANEOUS (ORIENTAL SORE).

LATYSHEV and KRIUKOVA (p. 296) give an account of the two types of oriental sore which have previously been differentiated in Turkestan. The first, Pendeh sore, is found in rural areas; its reservoir hosts are wild rodents (gerbils, marmots); it occurs chiefly in summer and autumn, has an incubation period of 3–6 months, and is relatively acute, with moist lesions in which parasites are scanty. The second, Ashkhabad sore, is a disease of towns; man is probably the reservoir, since rodents are absent; it is found throughout the year, has a longer incubation period, and is more chronic, with dry lesions in which parasites are numerous. In human inoculation experiments these two forms remain true to type.

LATYSHEV and KRIUKOVA (p. 24) have confirmed the Russian discovery that wild rodents are the reservoirs of *Leishmania tropica* in Turkmenia. The leishmania were proved infective by inoculation of man. They have found infection in 30 per cent. of *Rhombomys opimus* (up to 56·3 per cent. in November-December) and in a proportion of *Meriones erythrourus* and *Spermophilopsis leptodactylus*.

Phlebotomus species breed in the burrows of these wild rodents. Control of cutaneous leishmaniasis is best carried out by poisoning the burrows with chlorpicrine.

COLONIEU (p. 590) points out that oriental sore may be contracted anywhere in Algeria, even in Algiers itself. PARROT (p. 590) notes that *P. perfiliewi* (*P. macedonicus*) has been found in the outskirts of Algiers, together with several other species. It has previously been found in the Atlas mountains and other high places, and in many other countries round the Mediterranean and Black seas. In Italy it is regarded as a vector of oriental sore.

SENEKJI (p. 685) notes that in 22 cases of cutaneous leishmaniasis the formol gel test was negative. Intravenous injection of leptomonad forms of *L. tropica* in patients (suffering from general paralysis) who had a history of cutaneous leishmaniasis gave rise to fever which was followed by improvement in the mental condition. Two patients, immune to *L. tropica*, were injected with *L. donovani*, but kala azar did not develop. Similarly, no infection followed the injection of *L. brasiliensis* in a patient with a history of oriental sore.

MARCHIONINI (p. 125) in Ankara has found that early, typical, oriental sores respond well to local injections of 1–2 cc. of atebrin (10–20 per cent. solution). It may be necessary to repeat the injections at intervals of 8–10 days. For multiple sores atebrin may be given intramuscularly in doses rising from 0·1 to 0·3 gm., or intravenously. Chronic atypical ulcers do not respond well, and may require antimony injections or local applications of rivanol, trypaflavin, mercury or bismuth ointment, or electro-coagulation or deep X-ray. He notes that there may be no response to treatment unless concomitant malaria, lupus or syphilis have been treated. CUPI and CATTAPAN (p. 124) note that local injection of atebrin was successful in the treatment of oriental sore in Eritrea. MÉCHIN and GUIGON (p. 527) report some success, but not definite cure, in a case of oriental sore treated by infiltration with atebrin.

Having noted that local infiltration of oriental sore with atebrin may be followed by serious local reactions, VILANOVA (p. 828) experimented with a concentrated form of solustibosan, which contained 100 mgm. of pentavalent antimony per cc. instead of the usual 20 mgm. This was satisfactory, but the total dose for local infiltration should not exceed 2 cc. Injections into the sore are given once only; parasites disappear in 24 hours and the ulcer heals well in 2–3 months.

BOBROV (p. 441) treats Pendeh sore with dressings made by saturating cloth [presumably lint] with 5–10 cc. of the patient's own blood. These dressings are changed the following day and then renewed every 4–5 days. The ulcers usually heal in 2–3 weeks, and require 50–100 cc. of blood. In the later stages of healing, cod liver oil may be used in place of blood.

DUBOVSKY (p. 297) has used a vaccine of mixed strains of *L. tropica*, killed by heat, in the treatment of oriental sore in central Asia. The preparation of the vaccine from culture is described; it is given at first intradermally, and later subcutaneously. General reactions are rarely caused by the injections, but local effects, with inflammation, are common. Results in most cases are good.

ROW and KULKARNI (p. 378) have found that in old cultures of *L. tropica* there appear rounded leishmania forms of the parasites. These appear when the oxyhaemoglobin of the medium is transformed into methaemoglobin, and the authors have shown that the rounded forms

are found when young cultures are added to the fluid of old cultures, in which methaemoglobin is present.

Muco-Cutaneous (American).

Beltran and Bustamante (p. 441) have studied cutaneous leishmaniasis in the Yucatán peninsula. It is found only in the forest areas, and in the gum collectors who live in the forests, usually during the autumn. Incidence rates of 17 per cent. in men, 2 per cent. in women and 0·7 per cent. in children were found, but there is no information as to the method of infection.

Fuller and Geiman (p. 230) have been able to infect the Texas ground squirrel (*Citellus tridecemlineatus*) with *Leishmania brasiliensis*, the parasite of S. American muco-cutaneous leishmaniasis.

Pessôa and Coutinho (p. 762) found 21 sandflies infected with *L. brasiliensis* in 9,273 examined in the State of São Paulo, Brazil. *Phlebotomus migonei, P. pessoai* and *P. whitmani* were positive, and *P. whitmani* and *P. fischeri* were experimentally infected from monkeys.

Garzon and Molina (p. 125) report considerable improvement in a case of American muco-cutaneous leishmaniasis treated with intravenous tartar emetic. *Charles Wilcocks.*

MALARIA.

Downs, W. G., Gillette, H. P. S. & Shannon, R. C. **A Malaria Survey of Trinidad and Tobago, British West Indies.** *Supplement to J. National Malaria Soc.* Tallahassee, Fla. 1943, Aug., v. 2, No. 1, 1–44, 12 maps & 1 chart. [21 refs.]

This survey report opens with a condensed but adequate description of the topography, geology, meteorology and hydrography of Trinidad and Tobago. The climate is tropical and displays little diversity save seasonal changes in rainfall. Even in the dry season, January to May, the humidity approaches saturation point from midnight to dawn. The prevailing wind is from the east, the Trade Winds, and the heaviest rainfall occurs on the north-eastern, eastern and north central parts of Trinidad which are most exposed to these moisture-laden winds. There are several large swamps in Trinidad, the largest being the Caroni Swamp in the north-west of the Island, south-east of the capital, Port of Spain, and the Nariva Swamp near the middle of the east coast. The swamps are largely overgrown with mangrove : there is some cultivation of rice in swampy areas.

The population of Trinidad and Tobago according to the 1931 census was 387,425 and 24,385. Since then there has been a great influx of labour and U.S. military and other personnel in connexion with the construction of United States military bases. The estimated population at the end of 1941 was 506,316. The population of the two largest towns, Port of Spain and San Fernando, was 70,334 and 14,353 respectively. The density of population in the remainder of Trinidad was 203 persons to the square mile, varying in the different counties from 242 in St. George to 28 in Mayaro. The density of population in Tobago was 210 to the square mile. Negroes and persons of Negro descent form nearly two-thirds of the population. Persons of East

Indian origin numbered 138,667 in 1931. There were about 5,000 Europeans and 5,000 Chinese. There has been a considerable admixture of races.

The general death rate for 1941 was 15·95 per thousand, to which malaria contributed 0·98, pulmonary tuberculosis 0·97, and enteric fever 0·26. Malaria cases, clinically diagnosed, reported by health officers in 1940 numbered 20,691. Of the 2,128 positive blood slides examined in the Government Bacteriological Laboratory in 1941 *P. falciparum* was found in 1,769, *P. vivax* in 345, and *P. malariae* in 14.

During the present survey 26,349 school children were examined for splenomegaly, about a quarter of the total number of children in the colony of the age group 5 to 15. Enlarged spleens were found in 2,224, a spleen rate of 8·4. The county spleen rates varied from 53·1 in St. David, in the north-east corner of Trinidad, 37·5 in Mayaro in the south-east corner, and 33·1 in St. Andrew, on the east coast, to 3·4 in San Fernando on the west coast. The spleen rates in towns were: Port of Spain 1·7 and San Fernando 1·8.

The parasite rates of these school children varied directly with the spleen rates. For the colony as a whole 52·5 per cent. of the children with enlarged spleens harboured parasites; 7·5 per cent. of children without enlargement of spleen were parasite positive. The relative incidence of species of malaria parasites was *P. vivax* 26·7, *P. malariae* 15·6 and *P. falciparum* 57·7 per cent. *P. malariae* and mixed infections are relatively more common in the more malarious areas. *P. vivax* infections are much more frequent among East Indians than among Negroes.

In Tobago but little evidence of malaria was found in the seven schools that are situated at an altitude of over 400 feet.

During the present survey 13 species of anophelines were found in Trinidad: *A. aquasalis, A. oswaldoi, A. albitarsis, A. neomaculipalpus, A. apimacula, A. mediopunctatus, A. nimbus, A. eiseni, A. bellator, A.* (*Arribalzagaia*) sp., *A. homunculus, A. anoplus* and *A.* (*Kerteszia*) sp. The last four species have not previously been reported from Trinidad. In Tobago three species were found, *A. aquasalis, A. neomaculipalpus* and *A. apimacula.*

A. aquasalis is the common coastal anopheline of both islands. It breeds in brackish water, along the fringes of mangrove swamps, in ditches in coconut and sugar cane plantations and in water penned up by sand bars. Larvae have been found in fresh water streams, as far as 10 miles inland, but the species is much more prevalent in coastal regions. Adults feed freely on animals and man; they leave house or stable at or before dawn. Oöcysts were found in 46 of 1,383 "wild caught" *A. aquasalis* dissected (3·3 per cent.) and sporozoites in 1 of 1,364 dissected.

A. bellator is plentiful in the heavy rainfall areas of central and northern Trinidad. It breeds in collections of water in bromeliads which heavily parasitize the immortelle trees which serve as windbreaks and shade for cocoa plantations. There are areas of cocoa cultivation in southern, south-western and north-western Trinidad where immortelle trees and bromeliads are both abundant but where *A. bellator* is either rare or absent. These areas have a much lower rainfall than have northern and central Trinidad where *A. bellator* is so excessively abundant. Adults bite man very freely; they may bite during the daytime. As many as 950 were collected in an hour and a half from four small boys sitting by the roadside. Females are most in

evidence in the evening at dusk. Of 1,263 *A. bellator* dissected, oöcysts were found in 10 (0·78 per cent.); no sporozoites were found. A cheap, practical method of control of *A. bellator* has yet to be found.

A. aquasalis and *A. bellator* are the only vectors that have been incriminated. In Tobago *A. aquasalis* is the only vector of importance. Of the remaining species only *A. oswaldoi*, *A. albitarsis* and *A. neomaculipalpus* occur in sufficient numbers to be important if infected; the numbers of these species dissected were not large; none was found infected. *A. albitarsis* was found to be very susceptible to infection with *P. falciparum*. There is a close correlation between the presence of malaria and the presence of one or both of the species *A. aquasalis* and *A. bellator*. About half the area of Trinidad is free from malaria. In some areas domestic animals appear to divert large numbers of *A. aquasalis* from biting man.

A. homunculus, *A. anoplus* and *A.* (*Kerteszia*) sp. are all bromeliad-breeding anophelines with similar habits to those of *A. bellator*, but they are much rarer than that species. *Norman White.*

FRAGA, J. Malaria em Paranaguá. (Inspeção preliminar). [**Malaria in Paranaguá; Preliminary Survey.**] *Folha Med.* 1943, Oct. 25, v. 24, No. 20, 183–8.

This preliminary survey report outlines the history of the nearly 400-year-old town of Paranaguá on the coast of Brazil about 26°S. It has a settled population of 12,600 and a considerable floating population. Its topography, housing and economic conditions, educational facilities, and sanitary and medical organization are described. The spleen index of 1,649 persons of all ages examined was 11·6 per cent. Blood examination of these persons revealed *P. vivax* in 148, *P. falciparum* in 25, *P. malariae* in 1, and mixed infections in 7, a parasite index of 10·9.

The anophelines found included *A. cruzi*, *A. bellator* and *A. oswaldoi*. The two former are predominant and are believed to be the responsible vectors. They breed in collections of water at the base of leaves of bromeliads which extensively parasitize local vegetation.

Norman White.

RASHINA, M. G. [**Malaria Parasite Carriers and their Control.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1943, v. 12, No. 3, 3-14. [In Russian.]

Under war conditions, involving considerable movements of the general population and troops, the danger of malaria spreading outside the endemic areas of the Soviet Union has increased considerably. In this connexion the rôle of symptomless carriers in the dissemination of malaria becomes especially important, since these cases usually escape notice, and little is known regarding the epidemiological significance of such infections. Moreover, preliminary surveys organized by the Central Institute of Malaria have shown that the carrier state in malaria is more common than was hitherto suspected. After discussing the general situation, the author suggests the following measures of control: (1) continued examination of patients for prolonged periods of time (up to two years in the case of benign tertian, and 12–14 months in malignant tertian); (2) systematic and repeated treatment of such

cases; (3) mass blood examinations of the population (both healthy persons and patients); (4) increased use of mosquito netting.

C. A. Hoare.

DAVIES, R. A. **Observations on the Breeding of** *Anopheles* (*Anopheles*) *claviger*, **Meigen.** *J. Trop. Med. & Hyg.* 1943, Dec.–1944, Jan., v. 46, No. 6, 71–6, 6 figs.

The author has bred *Anopheles claviger* (*bifurcatus*) through several generations in cages, which has not previously been done.

Several other workers have shown that light (of some particular intensity and direction) may be effective in inducing mosquitoes and other Nematocera to perform a nuptial dance and then copulate. The author made a cage 5 feet long horizontally, by 1 by 1 foot, and put in it a dozen or so *A. claviger* bred from wild larvae, the females having previously fed on man. Outside the end of the cage he placed a 25 watt electric lamp, at dusk. The males danced in the part of the cage near the lamp, females entered the swarm, pairing took place and fertile eggs were laid. Without the lamp successful pairing did not occur. The work was done in an unheated room at about 12°C., and was repeated several times, and over several generations. It was a matter of indifference whether the mosquitoes were fed on man or rabbit.

Working with a water bath it was shown that the total length of aquatic life of the same species (from laying of egg to emergence from pupa) is about 76 days at 10·5°C., 33 at 18°C. The larvae were fed on powdered biscuit and yeast tablet.

P. A. Buxton.

MELNIKOVA, Z. A. *Anopheles bifurcatus* **in Kara-Kala in the Early Spring.** *Med. Parasit. & Parasitic Dis.* Moscow. 1943, v. 12, No. 1, 56–9. [In Russian.]

RAJINDAR PAL. **On the Bionomics of** *Anopheles culicifacies* **Giles. Part I. Longevity under Controlled Conditions of Temperature and Humidity.** *J. Malaria Inst. of India.* 1943, June, v. 5, No. 1, 77–85, 3 charts. [23 refs.]

The author defines the length of life of *A. culicifacies* under controlled conditions in the laboratory, and attempts to relate his data to numbers of adults captured at different seasons, in the Punjab.

The laboratory work was done by breeding from eggs laid by wild females. The adults bred in this way were given a single feed on man and put in a small cage in a desiccator, with mixtures of sulphuric acid and water to control humidity. The desiccators were kept in thermostats. It seems that at 25°, 30° or 35°C. (77°, 86°, 95°F.) the insects survived longer at moderate humidities (60 or 80 per cent.) than in saturated air, an interesting but unexplained observation. The total number of insects used at each point was small, and the statistical validity of the conclusions might well be considered. A proportion of the mosquitoes survived one hour at 41°C., none at 42°C. None survived one hour at −2°C., but the zone between that temperature and 12·7° was not explored. The latter temperature, which corresponds roughly to winter temperatures in the Punjab, was favourable to the survival of adults in desiccators. Adults and larvae could both be found in winter in nature.

P. A. Buxton.

ROY, D. N. **The Rôle of *Anopheles subpictus* Grassi as a Carrier of Malaria.** *J. Malaria Inst. of India.* 1943, June, v. 5, No. 1, 117–21. [19 refs.]

Larvae and adults of *A. subpictus* were collected from the salt-lake areas adjacent to Calcutta. The adults were taken in cowsheds which, for the most part, are separated from dwelling rooms by thatched partitions which offer no obstacle to the passage of mosquitoes. Precipitin tests showed that 25 per cent. of 1,515 engorged females had ingested human blood. This figure is very much higher than any recorded in previously published observations; most reports have stated that the species is almost exclusively zoophile.

Batches of *A. subpictus* were fed on *P. malariae*, *P. vivax* and *P. falciparum* gametocyte carriers, control tests being made in each case with *A. stephensi*. The oöcyst and sporozoite rates were 29 and 7 per cent. respectively, as compared with 50·9 and 45·3—the *A. stephensi* rates. Laboratory studies of the longevity of *A. subpictus* showed that in Calcutta 16 per cent. of naturally fed females survived a period of 10 days during January and February. The author concludes that though in the more humid parts of India naturally infected *A. subpictus* may be encountered, the danger of the species from the point of view of malaria transmission is negligible. *Norman White.*

SUNDARESAN, B. & RAO, M. A. **The Distribution of *Anopheles sundaicus* in Vizagapatam District; with Notes on certain Points of Differentiation between the Larvae of *A. sundaicus* and *A. subpictus*.** *J. Malaria Inst. of India.* 1943, June, v. 5, No. 1, 107–12, 1 map.

GAST GALVIS, A. Biologia y distribución geografica de los Anophelinos en Colombia. [**Biology and Distribution of the Anophelines of Colombia.**] *Rev. Facul. de Med.* Bogotá. 1943, Aug., v. 12, No. 2, 53–103, 11 figs. & 5 maps. English summary.

KEKHCHER, O. M. [**The Duration of Malarial Infection in Man, according to Information at the Sochi Malaria Station.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1943, v. 12, No. 2, 3–8, 2 charts. [In Russian.]

The author discusses the high incidence of relapses and chronic cases of malaria, which continue to be recorded in local registers, in spite of a general decrease in the incidence of fresh cases as the result of the successful application of antimalarial measures. This discrepancy is attributed to an exaggerated idea among medical officers regarding the duration of malarial infections, with the result that reinfections are interpreted as relapses, while various other ailments occurring in persons with a history of malaria in the past are diagnosed as chronic malaria without any objective criteria [see also this *Bulletin*, 1944, v. 41, 258].

On the other hand, observations based on the determination of the number of fresh cases have shown that in the Soviet Union the duration of benign tertian malaria does not, as a rule, exceed 12–18 months, while that of subtertian is from 2 to 12 months [see this *Bulletin*, 1943, v. 40, 345].

Similar observations were made by the author, who studied the records of the Sochi Malaria Station (Caucasus) where detailed registers, entered by a competent malariologist, have been kept since

1922. A statistical analysis of 5,504 case histories showed that the majority of patients (89–94 per cent.) recovered in the course of the first year of the infection. In individual cases (0·9–4·1 per cent. of 4,266) benign tertian malaria lasted 3–4 years, while only 0·16 per cent. of 1,037 subtertian cases manifested symptoms during the second and third years. The course of quartan malaria was similar but the small number of cases (107) does not warrant general conclusions regarding this disease. *C. A. Hoare.*

BAUM, G. **Latent Malaria presenting as Anaemia.** [Memoranda.] *Brit. Med. J.* 1944, Feb. 26, 289–90.

The author of this note writes from Khartoum and describes two cases in which anaemia (red cell counts of 3·64 and 2·9 millions respectively, with colour indices of 1·2 and 1·0), not susceptible to treatment with iron, cleared up promptly after a course of antimalarial treatment. Each patient had previously had malaria, but in each the blood was persistently negative, except that the first man had an attack of pyrexia during which subtertian parasites were found; it was this attack which led to the substitution of antimalarials for the (ineffective) iron preparation. *Charles Wilcocks.*

WHITEHILL, R. **Cerebral Malaria. A Case Report.** *Bull. Johns Hopkins Hosp.* 1943, Oct., v. 73, No. 4, 265–74, 1 chart.

This very detailed case report is not amenable to summary. The patient, a 25-year-old white male, was infected with *P. falciparum* in Guadalcanal. He was evacuated to New Hebrides. In spite of having received what is usually considered to be adequate specific treatment with both atebrin and quinine he developed symptoms of cerebral malaria some five weeks after the initial attack of malaria. He also developed symptoms of acute glomerular nephritis. He eventually made a complete but by no means an uneventful recovery. Intravenous quinine was administered. The author considers this to be the treatment of choice in the patient who is comatose from cerebral malaria. At one stage of the illness it seems probable that part of the haematuria was caused by quinine. The substitution of atebrin for quinine and plasmoquine was followed by a steady diminution of the haematuria. The opinion is expressed that the patient had a true malaria nephritis, caused by blocking of the glomerular capillaries with malaria parasites. *Norman White.*

KNEEDLER, W. H. **Malignant and Atypical Malaria.** Reprinted from *Clinics.* 1943, Dec., v. 2, No. 4, 809–27. [24 refs.]

This is a comprehensive account of the signs and symptoms that may result from infection with *P. falciparum*, more especially the pernicious forms of subtertian malaria. Much attention is paid to the differential diagnosis of malignant malaria especially in the presence of symptoms simulating those of some quite other pathological condition. In the treatment of pernicious cases the author expresses a preference for quinine in the initial stages followed by a course of atebrin after the pernicious symptoms have been brought under control. The first dose of quinine should be intravenous (10 grains of quinine dihydrochloride in 200 cc. of normal saline injected in not less than 15 minutes).

Subsequent injections may be intramuscular, which are almost as good even for the first injection (10 grains of quinine hydrochloride in 2 cc. of water, or at most 15 grains in 3 cc.). There is never any indication for intravenous atebrin since only small doses are advisable by this route, and the large initial doses necessary in malignant attacks can effectively be given intramuscularly. If atebrin be used in coma cases 0·4 gm. in 10 cc. water is given intramuscularly, half in each buttock, then 0·2 gm. seven hours later, and repeated 12 hours after that and then every 18 hours while the coma continues. Useful indications are given for the ancillary treatment of the more prominent symptoms. *Norman White.*

EPSTEIN, E. G. [**Treatment of Malaria with a Massive Initial Dose of Acriquine.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1943, v. 12, No. 3, 18–24. [In Russian.]

At present the standard method of treatment of malaria with acriquine (=atebrin, mepacrine), adopted in the Soviet Union, is a three-cycle course of 5–3–3 days, with intervals of 10 days between the cycles, the daily dose for adults being 0·3 gm. Under war conditions it was desirable to modify the treatment so as to obtain the maximum effect in the shortest time, without increasing the amount of the drug used.

A method of treatment on these lines was adopted by the author, after successful tests in 120 cases. The course consists of a large dose (0·5–0·6 gm. given in two portions) administered on the first day of the first cycle; this is followed by the usual dose (0·3 gm.) daily on the second, third and fourth days in succession, leaving the fifth day without treatment. Presumably, the standard course was followed in the remaining cycles.

The new method of treatment proved to be more effective than the standard one, both in benign tertian and subtertian cases, attacks of fever terminating 24 hours earlier than previously (in 1·2–1·8 days), without any toxic effects or relapses. [Similar high initial dosage has been used by British workers, see this *Bulletin*, 1942, v. 39, 666; 1943, v. 40, 821.] *C. A. Hoare.*

KAHLER, O. H. Beitrag zur Atebrinprophylaxe und Behandlung der Malaria. [**Contribution to Mepacrine Prophylaxis and Treatment of Malaria.**] *Deut. med. Woch.* 1943, Sept. 3, v. 69, No. 35/36, 630–31.

Two cases are described of unusual reactions to the prophylactic (suppressive) and therapeutic administration of mepacrine (atebrin).

Case I.—Exposed to malaria in South Russia, but received prophylactic mepacrine in the usual dose [? 0·06 gm. daily]. At the end of the season he received 0·1 gm. mepacrine thrice daily for five days, ending on October 14th, 1942. On October 13th and 14th he felt feverish and on October 16th an attack of benign tertian malaria developed, with parasites in the blood. He was given 0·3 gm. by intramuscular injection daily on October 17th, 18th and 19th; on October 20th 0·1 gm. was given three times by mouth. On the evening of that day, curious cerebral symptoms developed. The patient became forgetful and unable to concentrate, although consciousness remained clear. These

symptoms lasted for an hour on each evening of October 20th to 23rd, and then ceased. Mepacrine was discontinued on the evening of October 21st. The blood was free from parasites on October 27th.

Case II.—A man previously infected with benign tertian malaria, parasites being demonstrated in April 1942. Since June 1942 he took prophylactic mepacrine regularly. On October 11th he felt feverish. On October 12th and 13th he took 0·1 gm. thrice daily. On the evening of October 13th a clinical attack occurred although no parasites could be found in the blood. The mepacrine was discontinued for diagnostic reasons, and on October 16th benign tertian parasites were demonstrated. From October 17th onwards he was given 0·3 gm. intramuscularly daily for four days, and then the same amount daily by mouth for three days. Plasmoquine (pamaquin) was given for three days ending on October 28th. On October 27th the blood was free from parasites. The temperature continued to be unsteady until November 1st when another rigor occurred. The patient was then given quinine and no further attacks occurred.

Attention is directed to :—

(1) The onset of a malarial attack so soon after prophylactic and therapeutic courses of mepacrine (Case I). This is an exceptional case, which should not throw doubt on the usual antimalarial action of mepacrine.

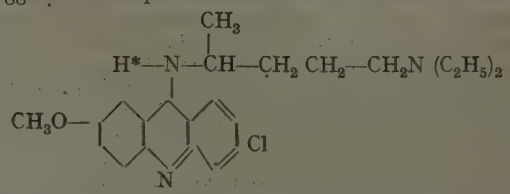
(2) The occurrence of cerebral symptoms due to mepacrine ; again, it is most unusual for such symptoms to follow the standard courses of treatment.

(3) Failure of the temperature to respond quickly to mepacrine by returning to the normal level. [These cases are exceptional, and should not cause unbelief in the efficiency of the antimalarial action of mepacrine in the great majority of cases. In the absence of data concerning the plasma concentration of mepacrine, it is difficult to decide the cause of these failures to respond to the drug.] *F. Hawking.*

Scudi, J. V. & Jelinek, Viola C. **Urinary Excretion Products of Atabrine.** *J. Biol. Chem.* 1944, Jan., v. 152, No. 1, 27–37, 4 figs.

The urine of dogs receiving mepacrine (atabrine) was collected and four fractions containing basic acridines, designated A, B_1, B_2, and C, were separated out according to their solubility in isoamyl alcohol, benzene, and other organic solvents.

Fraction A contained unchanged mepacrine dihydrochloride. Evidence obtained from the absorption spectra at *p*H 2·1 and 8·55 respectively suggests that mepacrine exists in two tautomeric forms,



the hydrogen marked by an asterisk oscillating between the nitrogen atoms on either side of the acridine group. Fraction A also contained an orange-yellow material, not fluorescent, probably not acridine, but not occurring except when mepacrine is given. Fraction B_1 contains

an acridine compound much like mepacrine but probably possessing a phenolic group —OH. It is suggested that this has replaced the methoxy group CH_3O—.

Fraction B_2 contains another derivative of mepacrine in which the basic side chain may have undergone partial degradation.

Fraction C contains another derivative of mepacrine which probably contains a phenolic group ; it shows no schizonticidal activity when tested against avian malaria and it is more toxic than mepacrine.

This group of isoamyl alcohol-soluble acridine bases, excreted in the urine, accounts for only about 5 per cent. of the mepacrine ingested. Only small or negligible amounts are excreted as water-soluble acridines of the ethereal sulphate or glucuronide type. In the case of the rest of the dose, the acridine ring is presumably broken down. Of the 5 per cent. excreted by the dog as acridine derivatives, 25 per cent. is unchanged mepacrine, 2–5 per cent. consists of Fraction B_1 and 2–5 per cent. as Fraction B_2, and the rest as Fraction C. Rats excrete about 2 per cent. of the dose within 24 hours ; 90 per cent. of the acridine excreted is unchanged mepacrine, none is B_1, 2–5 per cent. is B_2 and 2–5 per cent. is C. In a sample of human urine, there was as much Fraction C as unchanged mepacrine. In rabbits, the proportions excreted are different again.

[This paper contains extensive chemical information which should be consulted in the original by those interested.] *F. Hawking.*

Brodie, B. B. & Udenfriend, S. **The Estimation of Atabrine in Biological Fluids and Tissues.** *J. Biol. Chem.* 1943, Nov., v. 151, No. 1, 299–317, 4 figs.

Mepacrine (atabrine) is extracted from the biological fluids by suitable organic solvents and its fluorescence under ultraviolet illumination is measured in a suitable fluorometer. The No. 12 Coleman electronic photo-fluorometer is recommended, with a 2 mm. No. 5113 Corning glass filter (Coleman B4) to isolate the activating energy, and a Corning No. 3385 filter (Coleman PC9) to limit the transmission of the resulting fluorescent light.

Procedure.—" Add 3 ml. of 0·2 M Na_2HPO_4 and 30 ml. of ethylene dichloride to 1 to 10 ml. of biological material in a 60 ml. glass-stoppered Pyrex bottle (blood is first hemolyzed with 2 parts of water). Shake vigorously for 5 minutes, preferably on a shaking apparatus. Decant into a 50 ml. centrifuge tube and centrifuge for 10 minutes at moderate speed to break the emulsion. Remove the supernatant layer by aspiration. A solid gel sometimes forms in the ethylene dichloride which may be broken by vigorous stirring with a glass rod. A second centrifugation at high speed will then produce a clean separation of the two phases. Return the ethylene dichloride solution to the original rinsed out bottle, restraining the coagulum with a stirring rod. Add an equal volume of 10 per cent. NaOH and shake for 3 minutes. Remove the major portion of the sodium hydroxide solution by aspiration and transfer the remainder of the contents of the bottle to a narrow test-tube. Centrifuge for 1 minute. Remove the supernatant layer by aspiration, wash the sides of the tube with water, and remove the water by aspiration. Pipette exactly 20 ml. of the ethylene dichloride into a prepared glass-stoppered bottle, add 1 ml. of water and 10 ml. of 85 per cent. lactic acid, and shake vigorously for 5 minutes. Transfer to a prepared, narrow 35 ml. centrifuge tube and centrifuge for 1

minute at moderate speed. Transfer at least 8 ml. of the aqueous phase to a matched cuvette and determine its fluorescence in relation to a properly prepared standard."

"The sensitivity of the fluorometer is calibrated by an atabrine standard prepared in lactic acid. The standard used in the routine estimation of atabrine during ordinary atabrine administration to humans is prepared as follows: Add 1 ml. of solution containing 0·5γ [microgramme] of atabrine to 10 ml. of 85 to 90 per cent. lactic acid. A mixture of 10 ml. of lactic acid and 1 ml. of water is used for the blank setting of the instrument. The manifest fluorescence of atabrine is a linear function of its concentration in the range usually encountered when the measurement is made with a suitable fluorometer. Consequently, the calculation of atabrine concentration is by direct proportion." In estimations of blood and plasma the alkali wash may be omitted.

By this method amounts of mepacrine as low as 0·1 microgramme (absolute) may be estimated within an error of less than 5 per cent. A single extraction method is also described, which is simpler and more rapid than the above, but less sensitive. It estimates down to 0·5 microgramme, but in plasma and whole blood it gives a blank reading of 2·4 microgrammes per litre, so it is not recommended for plasma estimations because of the low concentration of mepacrine commonly observed in plasma. In the metabolism of mepacrine, degradation products are produced, some of which are fluorescent; but the above methods isolate the unchanged mepacrine from such products and the error from this source is small.

[The paper contains many technical details which cannot be reproduced in an abstract and the original should be consulted by those interested. The methods described have been utilized very extensively to study the blood concentration of mepacrine under many different circumstances and much valuable information has been obtained. The estimation of mepacrine in blood or plasma is a very intricate procedure, which can be carried out only in specially equipped and trained laboratories. Estimation in urine is a relatively simple procedure.]

F. Hawking.

Kohlschütter, E., Zipf, H. F. & Triller, G. Zur Toxikologie der Malariamittel Plasmochin, Atebrin, Certuna und Chinin. [**The Toxicology of the Antimalarials, Pamaquin, Mepacrine, Certuna and Quinine.**] *Arch. f. Exper. Path. u. Pharm.* 1943, May 24, v. 201, No. 4, 402–16.

The authors' observations were made during studies of the therapy of *P. gallinaceum.* They used fowls 2–6 months old weighing about 700 gm. The drugs were given by sound into the stomach.

Pamaquin.—This compound caused early deaths (in less than 24 hours) or, in smaller doses, late deaths. In the latter case, reddening of the intestinal mucous membrane and pancreas were present, together with diarrhoea and the passage of undigested food in the faeces. A large dose of 120 mgm. per kgm. (given to a single fowl) caused somnolence and other symptoms of depression of the nervous system, going on to tremor, clonic convulsions, coma and death in seven days. Doses of 71–85 mgm. per kgm. caused death in 5–72 hours with similar symptoms. Doses of 20–28 mgm. per kgm. caused, in three out of four birds, similar symptoms of somnolence, together with

curious functional disturbances in the act of pecking. Lower doses caused paralysis of the lower eyelid in some birds. Judging from small groups of birds, the minimal lethal (single) dose is about 57 mgm. per kgm.

Certuna produced symptoms similar to those caused by pamaquin. The birds showed marked neurotoxic symptoms as above. The labyrinthine reflexes were suppressed and the light reflex much diminished. With both compounds, the nervous symptoms prevented the ingestion of food and many of the deaths were hastened by starvation. As with pamaquin, evidence of intestinal irritation was present. The lethal dose was about 60 mgm. per kgm.

Mepacrine caused death mostly within 24 hours, sometimes delayed up to three days. The symptoms consisted of depression of the nervous system (somnolence, failure to eat, etc.) but the convulsions and curious disturbances due to the previous two compounds were absent. Diarrhoea with yellow stools occurred. The lethal dose was about 710 mgm. per kgm.

Quinine hydrochloride caused death quickly (within 1¼ hours) or not at all. The bird became unsteady in its stance and movements. Sometimes convulsions occurred. Finally somnolence and coma developed, and death occurred from respiratory failure. The lethal dose was about 860 mgm. per kgm.

Repeated doses.—In one series, with few birds, the dose was given daily for five days. For pamaquin and certuna the lethal dose was about 14 mgm. per kgm., for mepacrine about 280 mgm., and for quinine about 570 mgm. The symptoms were as described above but somnolence was more marked and disturbances of function less marked.

In another series, a small dose was given daily until marked symptoms or death occurred (*e.g.*, 24 days). With pamaquin and certuna, symptoms similar to those described above occurred, *e.g.*, somnolence, functional disturbances, etc. With mepacrine, general depression of activity developed, together with general yellowness of exposed parts, but there was no diarrhoea. Quinine, in repeated moderate doses, caused some loss of weight but no deaths.

The brains of birds which had shown nervous symptoms were examined histologically. In those dying after pamaquin, certuna or quinine, no lesions were discovered. After mepacrine there were distension of some of the blood vessels, some small haemorrhages on the surface of the cerebrum, and a little perivascular infiltration of small round cells. It is considered that the paralysis of the lower eyelid, observed in some birds, was due to a lesion of the oculomotor nucleus, although there is no anatomical evidence to this effect.

It is emphasized that the symptoms produced in birds by the toxic action of these drugs are different from those produced in man.

F. Hawking.

COVELL, G. & JASWANT SINGH. **Antimalaria Operations in Delhi. Part IV.** *J. Malaria Inst. of India.* 1943, June, v. 5, No. 1, 87–106, 8 charts. [10 refs.]

Regional epidemics of malaria in Northern India are apt to recur at intervals of several years. Such a severe regional epidemic affected large areas of the Punjab, United Provinces and Delhi Province in the second half of 1942. The previous epidemic year was 1933; the nine-year interval between the epidemics was unusually long and the

communal immunity was consequently unusually low. The present report describes the malaria experience of the Delhi urban area during the epidemic and attempts to assess the adequacy of the antimalaria organization set up in Delhi in 1933.

The monsoon rainfall in Delhi had been below the average of 22·6 inches during each of the five preceding years; in 1941 the total rainfall was only 9·7 inches. In 1942, 29·8 inches fell between June and September, 32 per cent. above normal. Very extensive flooding occurred throughout the riverain tract of Delhi Province and the Jumna River was at flood level over an exceptionally protracted period. The antimalaria protective bunds remained unbreached, but eventually water percolated through the low-lying ground behind the bunds. By the middle of August there were extensive sheets of water in the protected area, affording ideal breeding grounds for *A. culicifacies*. High humidity favoured the longevity and activity of mosquitoes. The population of the urban area was increased by military personnel, refugees from flooded areas (many of whom were infected on arrival), coolies engaged on constructional work, and 2,500 internees in the Purana Qila, where effective protection from malaria was impossible.

The number of malaria cases treated in the dispensaries of the urban area was 26 per cent. less than in 1933 though the population in 1942 was 50 per cent. higher. In the Gurgaon District of the Punjab, which adjoins Delhi Province, dispensary attendances for malaria were eight times higher in 1942 than in 1941; in the Delhi urban area they were little more than twice as great. The chief emergency measure adopted was the spray-killing of adult mosquitoes. A petrol-driven power sprayer was very effective. An indication of the efficacy of this measure is afforded by the fact that the infectivity rate of *A. culicifacies* was lower, 0·5 per cent., than in the inter-epidemic period (10,000 dissections) whilst the percentage of *A. culicifacies* that had fed on human blood was very much higher. It is considered that the intensity of the epidemic was greatly reduced as the result of the elimination of potential mosquito breeding places by the permanent engineering works carried out during the previous five years. [For earlier reports on Antimalaria Operations in Delhi see this *Bulletin*, 1939, v. 36, 917; 1940, v. 37, 747, and 1942, v. 39, 259.] *Norman White.*

Russell, P. F., Knipe, F. W. & Sitapathy, N. R. **Malaria Control by Spray-Killing Adult Mosquitoes: Fourth Season's Results.** *J. Malaria Inst. of India.* 1943, June, v. 5, No. 1, 59–76, 2 figs. on 1 pl.

The report by the first two authors on the third season's results obtained in the control of malaria in South Indian villages, where *A. culicifacies* is the only vector, by spray-killing adult mosquitoes, was summarized in this *Bulletin*, 1942, v. 39, 667. The fourth year's observations now recorded fully confirm those of previous years: spraying houses, animal sheds and buildings with pyrethrum insecticides reduces malaria transmission to a remarkable degree.

A further study was made of the most effective types of spraying apparatus suited to local conditions, and further modifications were made. A detailed description is given of an improved hand atomizer; a hand-pumped pressure tank; a power-filled pressure tank; a power-operated "two man" pressure outfit, and a "one-man" power-operated pressure outfit [this *Bulletin*, 1943, v. 40, 116]. The labourers

employed all expressed a preference for the hand-pumped pressure tank type of equipment to all others tried.

The use of Indian-grown pyrethrum in the preparation of the insecticide has reduced the cost of spraying [this *Bulletin*, 1943, v. 40, 14]. Information regarding the preparation of a water emulsion of a locally extracted pyrethrum is given.

Seven villages were sprayed in the 1941 season ; their populations varied from 88 to 7,620. The method of applying the insecticide varied in the different villages. The decline in the parasite rate and the reduction in the size of spleens was marked in all cases. In six untreated villages parasite rates were uniformly higher in 1941 than they had been in 1937. In Kasangdu, population 1,790, the parasite rate had been reduced from 57 to nil as the result of three seasons' spraying and there were no larger spleens than size 1. This village was not sprayed in 1941 ; the parasite rate rose to 15 per cent. and there were several size 2 spleens. In one village every person was given a preliminary treatment with plasmoquine before spraying began ; the subsequent decline in the parasite rate was no greater than could have been achieved by spraying alone. The villagers like spray-killing and appreciate the benefits it confers ; they gave excellent co-operation. The cost per person for the 1941 season varied in the different villages from 3 to 7½ annas. The size of houses, the distance between houses, and the number of animal shelters, influence the cost per person.

Norman White.

ANNECKE, S. **Repellents in Malaria Control.** *South African Med. J.* 1943, Dec. 25, v. 17, No. 24, 383–6.

The method of experiment is not fully described but it appears to have consisted in having human subjects in a series of huts into which *Anopheles gambiae* and *funestus* could enter freely and then at intervals during the night collecting and counting the mosquitoes that had entered the huts, the proportion of males and females, and the number which had fed. Huts with control subjects were compared with those whose occupants were treated with various repellents. The author concludes that plain citronella oil still holds first place as a repellent provided it is applied at three-hourly intervals. Tagetes oil and lard were of no value. A cream containing naphthalene and a concentrated extract of pyrethrum (the precise formula is not given) was almost equal to the citronella if re-applied every three hours. If the huts were dusted with pyrethrum powder (¼ oz. per 100 sq. ft. at intervals of five hours) the number of mosquitoes feeding was still further reduced (to about one-third of the figure for huts occupied by citronella-treated subjects). *V. B. Wigglesworth.*

SUBBARAMAN, A. K. & VEDAMANIKKAM, J. C. **Trimming the Edges of Breeding Places near Human Habitations as an Antilarval Measure.** *J. Malaria Inst. of India.* 1943, June, v. 5, No. 1, 113–15, 1 fig.

The observations recorded were made in the Wynaad, S. India. It was shown that the removal of vegetation along the banks of a stream, trimming the edges of the stream with a spade, and the removal of loose stones and weeds projecting above the water surface along the edges of the stream, were sufficient to eliminate entirely the breeding of

A. fluviatilis, the local vector, and of other species as well. Thereafter weekly inspections and maintenance of the work are essential, but the control measure is cheap. *Norman White.*

ADISUBRAMANIAM, T. S. & VEDAMANIKKAM, J. C. **The Relationship between the Breeding Places of *A. fluviatilis* and Human Dwellings and its Significance in limiting the Scope of Antilarval Measures.** *J. Malaria Inst. of India.* 1943, June, v. 5, No. 1, 53–8, 2 maps.

The inhabitants of the Wynaad (S. India) live in small groups of huts along the margins of the valleys. In these valleys *A. fluviatilis*, the local vector, breeds in streams and irrigation channels. The observations recorded were made in two villages, Kalpatta and Sultan's Battery. All the channels forming breeding grounds in the neighbourhood of these two villages were measured off into 100 feet sections. Collections of larvae were made in each section once a week. The density of *A. fluviatilis* larvae was found to vary inversely with the distance of the section from human habitations. The maximum density was always within 1,000 feet of such dwellings. The control of breeding by oiling along 1,000 feet in one of the areas resulted in a marked decrease in the number of adults caught in the nearby huts, as compared with the previous year when no control measures were in force. The authors conclude that antilarval measures against *A. fluviatilis* may be limited to breeding places within 1,000 to 1,500 feet of the dwellings they are designed to protect. *Norman White.*

ADLER, S. & TCHERNOMORETZ, I. **Development of Gametocytes from Extra-erythrocytic Forms in *Plasmodium gallinaceum*.** [Correspondence.] *Nature.* 1944, Jan. 15, 83.

The authors refer to their original work [this *Bulletin*, 1942, v. 39, 524] in which they showed that in fowls inoculated with emulsions of organs containing exo-erythrocytic forms of *Plasmodium gallinaceum*, or subjected to the bite of *Aëdes aegypti* infected with that parasite, intense and continuous quinine treatment prevents the formation of pigmented parasites, but allows the extra-erythrocytic forms to persist. These forms do not develop further while quinine is given in high dosage, but if it is stopped they undergo normal development in red cells. The authors have now shown that some of these exo-erythrocytic forms invade red cells and develop directly into gametocytes, and that young gametocytes can be recognized 27½ hours after cessation of quinine; they approach their maximum size before the first cycle of erythrocytic schizogony is completed.

Charles Wilcocks.

JACOBS, H. R. **Immunization against Malaria. Increased Protection by Vaccination of Ducklings with Saline-Insoluble Residues of *Plasmodium lophurae* mixed with a Bacterial Toxin.** *Amer. J. Trop. Med.* 1943, Nov., v. 23, No. 6, 597–606, 3 figs. [14 refs.]

Previous laboratory work on the subject of immunity in malaria indicates that the host elaborates certain kinds of defence against

infection. Under the heading of "species specific" immunity the following types may be recognized :—

1. Cellular immune defences : the macrophage system.
2. Humoral immune bodies : passive immunity.
3. Agglutinins : one element of humoral antibodies.
4. Specific absorption of immune bodies by parasites.

Under the heading "group-specific antibodies" are :—

1. Precipitins.
2. Complement fixing antibodies.

It is noteworthy that the immune phenomena of the first group are concerned with protection, and that they are the result of the interaction of whole parasites or their water-insoluble residues, while those of the second group are caused by the water-soluble material extractable from the parasites.

A further examination of available data indicates that the antigen which gives rise to protective antibodies has the following properties ;—

1. It is an inefficient stimulus to antibody formation.
2. It reacts readily with protective antibodies.
3. It is insoluble in ordinary aqueous media.

It would thus appear that the antigen is a partial antigen or hapten. In favour of this view are : the difficulty experienced by the host in bringing the primary malarial attack under control, and the tendency to relapse. These features are readily explained by the ineffectiveness of the antigen and the readiness with which the parasites combine with such antibodies as are formed. Added to these obstacles to the development of a satisfactory humoral immunity is the fact that for the greater part of its existence the malarial parasite is growing within the red blood corpuscle, where it is protected from adverse humoral influences.

In the experiments reported in this paper antigen material was prepared from red blood corpuscles of ducks infected with *Plasmodium lophurae*, by the addition of saline, sucrose and protamine sulphate. Finally, the sediment of black malarial material was washed several times in saline, and stored in saline containing one-half per cent. phenol. Ducks receiving 0·5 cc. of a heavy suspension of the protamine plasmodial precipitate, 20 or 10 days before an infecting dose of parasites showed a survival beyond the 20 days limit of survival of unvaccinated controls. Aqueous extracts of this material gave no protection, though the insoluble residue left over after exhaustive aqueous extraction with ball mill grinding gave a similar protection. The protective action of this insoluble residue, administered in five doses on the 19th to the 3rd day before the injection of the infective dose of parasites, was definitely increased when a quantity of staphylococcus toxoid was added to each dose just before administration. The results of these experiments are in agreement with the hypothesis that the useful malarial antigens are of the nature of insoluble haptens.

C. M. Wenyon.

TRYPANOSOMIASIS.

TANGANYIKA TERRITORY: DEPARTMENT OF TSETSE RESEARCH. **The Activities of the Department of Tsetse Research, Tanganyika Territory, since 1936.** 27 mimeographed pp. With 3 appendices. [n.d.]

The present report is a continuation of its predecessor the Tsetse Research Report 1935–1938 [this *Bulletin*, 1941, v. 38, 73] but includes a review of the work of those years as well as the more recent researches. [Reference to SWYNNERTON's volume *The Tsetse Flies of East Africa*, 1936, is of great assistance in understanding this difficult and complex subject; see this *Bulletin*, 1937, v. 34, 363.] A seven years programme of research was begun in April 1938 when grants of £208,000 from the Colonial Development Fund and £35,000 from the Tanganyika Government had been made. A meeting of officials—administrative officers and representatives of the agricultural, veterinary and medical departments—whose duties were closely associated with the tsetse-infested areas, was held at Tabora in 1937 and a programme of 19 schemes of investigation was approved. In June 1938, C. F. M. SWYNNERTON and B. D. BURTT, botanist, were killed in a flying accident, and H. E. HORNBY, the Director of the Veterinary Department, became Director of Tsetse Research. The outbreak of war caused a great reduction in the staff and the closing down of some of the schemes.

This report deals with the study of six of the eight species of *Glossina* known to exist in Tanganyika Territory, *viz.*, *G. morsitans*, *G. swynnertoni*, *G. pallidipes*, *G. brevipalpis*, *G. austeni* and *G. palpalis* var. *fuscipes*; each is considered separately.

In this work a close study has been made of the physiology and habits of the various species and of their environment—the vegetation, atmospheric conditions, soil, enemies, food supply, etc., and laboratory and field experiments have been carried out. The workers have critically examined the results obtained and discussed their meaning and importance.

G. morsitans.—C. H. N. JACKSON studied the fly population in an area of several square miles at Kakoma, about 70 miles south of Tabora; captured flies were marked with paint according to a special method [this *Bulletin*, 1937, v. 34, 539] and released, and from the proportion of recaptured marked flies he was able to estimate the size of the local fly population. The accuracy of the other method of estimating the numbers, by the catches on fly rounds, was confirmed; a catch of one old male fly per 10,000 linear yards represented a real density of about 7 or 8 old males per square mile. JACKSON also found that the male flies keep within an area of about one mile in diameter throughout their lives, except that there is a slow outward drift of flies which escape and establish themselves in other localities or ambits. The mean duration of life of the male flies is about four weeks, while females live considerably longer in Nature. Studies on breeding showed that even in the dry season over 90 per cent. of the pupae are scattered singly outside the recognized breeding sites.

Ants, chiefly of the genus *Pheidole*, destroy pupae, and this may possibly be facilitat d by prevention of grass burning, since such fire exclusion was found to be followed by a considerable decrease in the fly population.

Early burning of grass is followed by increased density of the vegetation ; an experiment of this kind at Abercorn in Northern Rhodesia gave disappointing results and was abandoned.

The report states that the war has interfered more seriously with the work on *G. morsitans* than with that on any other species. Discriminative clearing experiments should be made in several different types of *G. morsitans* country, and a fire-excluding experiment in typical Tanganyika " miombo " wooding should be begun again.

G. swynnertoni.—From his observations at Shinyanga JACKSON concluded that this species has a greater tendency to disperse than *G. morsitans*. Fire-exclusion experiments have been in progress for several years at Shinyanga and were described and discussed in the previous report by W. H. POTTS, senior entomologist ; he concluded that the considerable reduction in the fly population that occurred, although intensified by a succession of years unfavourable to the fly, would still have taken place without climatic help. NAPIER BAX made experiments on the senses of smell and sight of *G. swynnertoni* ; it reacted to the scent of oxen up to a distance of 180 feet but not at 300 feet ; man also attracted the flies but to a less degree. Black oxen were seen by the flies at 450 feet but not at 600 feet. Noise did not affect the flies. Physiological observations on the effects of the dry season, the heat of the sun and of the fly's activity were made by VANDERPLANK, POTTS and LLOYD respectively, and POTTS and VANDERPLANK carried out preliminary experiments on phototropism of *G. swynnertoni* and *G. morsitans* on the lines described by JACK and WILLIAMS [this *Bulletin*, 1938, v. 35, 338].

During the latter part of the rainy season *G. swynnertoni* seems to concentrate in the " hard pan " type of country, but in the dry season it spreads out and becomes more evenly distributed.

Observations were made to determine whether the movements of herds of game are important in the spread of tsetse flies and in affecting the numbers of flies caught from time to time ; JACKSON concluded that the passing of game (or cattle) through an area does not materially affect the numbers of flies caught afterwards.

Dissections of *G. swynnertoni* and *G. pallidipes* showed no statistically significant differences between the infections of males and females or between *G. swynnertoni* and *G. pallidipes* in regard to infections with *Trypanosoma brucei*, *T. congolense*, *T. vivax* or total infections.

It was found that a thicket barrier about 2½ miles long, two-thirds of which was formed by *Euphorbia tirucalli*, 100 yards deep, and the remaining third of its length by fire-excluded deciduous thicket, 300 yards deep, impeded the passage of *G. swynnertoni* but by no means formed a complete barrier. About three times as many marked flies were caught on the side of the barrier on which they had been marked and released as on the opposite side ; the passage of game through the barrier is thought to have aided the passage of the flies.

Fire-exclusion reduced the number of *G. swynnertoni* and caused them to concentrate in limited short-grassed areas, but in favourable years their numbers again increased ; the trees and thickets in these short-grassed (hard pan) areas were therefore felled and this resulted in a reduction from large numbers to very few flies ; the females, however, were still fertilized in normal proportions. It has not yet been determined in what way this clearing of trees and thickets caused the reduction.

Some observations on game, made with powerful field glasses, showed that giraffe and wart-hog were attacked by the flies but zebra were not, and the precipitin test confirmed the latter observation.

G. pallidipes.—This species, an important transmitter of infection to cattle, is thought to be much less attracted to man, the flies being caught on man only when numerous and when external conditions are severe. Both MOGGRIDGE at Kilifi, in the coastal area of Kenya Colony, and VANDERPLANK at Shinyanga found that the flies were most numerous in the wet season. Observations on the effect of temperature and atmospheric humidity were made at both places. *G. pallidipes* is found in various surroundings but appears to be especially associated with, and to some extent dependent on, thicket.

G. brevipalpis.—Comparatively few observations were made on this species of tsetse fly. It was found more in " miombo " forest than in dense thicket. It has crepuscular feeding habits but feeds very little at night, even in moonlight.

G. austeni.—MOGGRIDGE studied this fly at Kilifi under Kenya coastal conditions. Heat and a dry atmosphere greatly lowered its activity and compelled it to feed in the early morning and at night. It is thought that it finds its food at night by its sense of smell, since ELTRINGHAM showed that its eyes were not specially adapted for night vision. It deposits its larva near fallen logs and probably not outside such sites to any great extent. It was found in both miombo forest and in thicket but seems to prefer thicket and shows no tendency to spread into more open vegetation in the wet season.

G. palpalis var. *fuscipes*.—Observations on this species were made by LLOYD and GLASGOW during trapping and clearing experiments. Lloyd found that traps caught about 1½–2 per cent. of the estimated old male population per day at the end of the dry season. Three pairs of " boys," however, caught 10 times as many male flies as 66 traps did. The flies fed more on reptiles than on mammals and birds even when the latter were plentiful.

Clearing of the vegetation to a depth of about 100 feet from the water's edge caused a great reduction in the number of flies, though it did not interfere with their food supply and they still bred in the inland thicket.

The laboratory.—In the previous report, POTTS, FORD and VANDERPLANK described laboratory investigations including some work which could equally well be called field research. Identification of the kind of blood found in the tsetse flies had been made formerly by the precipitin test and by measurement of the red blood corpuscles. Both methods lack precision as they identify groups of animals rather than species. VANDERPLANK has introduced an agglutination test in which the blood in the fly is tested against a number of different animal sera; the serum with which no agglutination occurs indicates the source of the blood. The chief difficulty was the collection of sterile blood from wild animals for the preparation of the test sera. The results were promising but owing to certain difficulties which have not yet been overcome, the test has not been much used.

Other laboratory work included research on the following: rearing tsetse flies in the laboratory; the effect of oil paints on the fly; fertilization of females; the times of day of deposition of larvae and of emergence from pupae; the relation of the weight of the pupa to its vitality; the duration of pregnancy in the field; parasitization of pupae of *Glossina* by Bombyliids.

Appendices give lists of tribal reclamation work, of the 19 schemes of the seven years programme, of the publications by the research staff, and of conferences attended in connexion with the work. *J. F. Corson.*

CHORLEY, J. K. **Tsetse Fly Operations, 1942. Short Survey of the Operations by Districts for the Year ending December, 1942.** Reprinted from *Rhodesia Agric. J.* 1943, May–June, v. 40, No. 3, 174–7; also as *Bull. Ministry Agric.* [Southern Rhodesia] No. 1232, 1943, 4 pp.

During 1942 two important discoveries were made. A very heavy concentration of *Glossina morsitans* was found in Portuguese territory on the Busi River, about 6 miles from the border, and east of Chipinga; it was not surprising as the steady westward spread of this fly has been observed for several years [this *Bulletin*, 1944, v. 41, 269]. The other event was the discovery of *G. pallidipes* in the north-eastern part of the Wankie district and in the south-western corner of the Sebungwe district; hitherto it had been thought that *G. morsitans* was the only tsetse fly in the northern fly-belt. The area involved is known to be several hundred square miles, but it must be assumed that a far greater area is infested.

Two cases of human trypanosomiasis were found near Chirunde on the Zambesi River in the Lomagundi district; they are the first cases recorded from the Lomagundi fly-belt.

The position in the various areas—Darwin, Urungwe, Lomagundi, S.W. Gatooma, Sebungwe, Melsetter and Sabi Valley—is briefly reported. In the Melsetter (Eastern Border) area there were more cases of animal trypanosomiasis than in any previous year, 329 cases being diagnosed by blood smears; the disease was also more widespread, involving 38 farms.

A total of 25 tsetse (16 *G. pallidipes* and 9 *G. brevipalpis*) were caught on the Southern Rhodesia side of the border. *J. F. Corson.*

BAX, S. N. **A Practical Policy for Tsetse Reclamation and Field Experiment.** Reprinted from *East African Agric. J.* Nairobi. 1944, v. 9, 1–23, 8 figs. on 4 pls. & 1 folding map. [11 refs.]

By "reclamation" the author means measures taken to free land from tsetse flies or to protect land from invasion by them. The associated questions of anti-erosion measures, provision of water, control of grazing, &c., are not dealt with, though their importance in reclamation of land is fully recognized. About 1,000 square miles have been freed from tsetse flies in Tanganyika Territory during the last 20 years but, in the same period, thousands of square miles have become infested. In this paper the tsetse situations which can be remedied are described and the author says that the time has come when the knowledge gained by research should be applied. The goal to be aimed at—the ability to reclaim cheaply any kind of country from any species of tsetse—has not yet been attained, but a great advance has been made in the last 10 years and "the whole conception and emphasis of tsetse reclamation is changing."

It is estimated that about 4½ million square miles of the African continent are infested with tsetse; in Tanganyika Territory about two-thirds to three-quarters of the country is infested, in Kenya Colony about one-seventh and in Uganda about one-fifth. The problem is

complicated by the fact that there are ten species of *Glossina* in East Africa, of which four, *G. morsitans*, *G. swynnertoni*, *G. pallidipes* and *G. palpalis*, are the most important; each has its own mode of life, special habits and surroundings. The author describes various tsetse situations and what should be done to remedy them.

Contact between cultivation steppe and fly-bush.—[Cultivation steppe is defined as an open area under sufficiently close human occupation, agricultural, or agricultural and pastoral, to have been cleared of the greater proportion of its natural woody vegetation.] There are many causes of an advance of tsetse into cultivated land; the land may become worn out and so deserted; the population leaves an unpopular chief; water supplies fail; wild animals become too troublesome, &c. In addition to a gradual advance the fly is also able to leap forward several miles at once in certain circumstances, *e.g.*, over rocky land, abandoned land or land not fully occupied. For these conditions the author advocates the formation of "defence lines" of cleared boundaries in which the bush is cut back and cleared.

The thorn savanna infested with G. swynnertoni.—Discriminative clearing alone has been found effective for this situation. The tsetse fly requires a concurrence of different types of vegetation and it was found that cutting down the easily felled vegetation of the hard pan areas was sufficient to produce practical elimination of the tsetse. In the Ukerewe peninsula on Lake Victoria the clearing of 4,600 acres of hard pan rendered 75,500 acres (118 square miles) almost clear of tsetse and of sleeping sickness. Where areas of cultivated land or of other tsetse-free land are separated from one another by bands of fly-infested bush of moderate width, discriminative clearing of the latter may be applied with success.

Thorn savanna and "miombo" wooding infested by G. pallidipes.—Here it is recommended to remove the thicket on which this species is dependent.

The great plains carrying a lace-work of vegetation infested by G. swynnertoni and morsitans.—In the gall-acacia plains it is recommended to make a clearing, a mile wide, along the edge of the thorn bush, thereby forming a barrier between it and the plains, and to fell any small islands of breeding bush in the plains; this should be followed by the provision of water tanks to encourage cattle owners to settle there. These measures have been successful in reclaiming 160,000 acres (the Huru-huru plains) near Shinyanga. The maintenance cost is estimated at 1/80 man-day labour per acre per annum. A somewhat similar method is recommended for dealing with plains carrying other types of vegetation; discriminative clearing should be done under the direction of an experienced officer.

The linear habits of G. pallidipes, G. brevipalpis, G. austeni and G. palpalis.—The first three species are dependent, especially in the dry season, on the shade of bush along rivers and drainage lines; the other species, *G. palpalis*, haunts the borders of lakes and rivers. The remedy in the case of the first three species is cutting out the undergrowth, leaving only the large, clean-stemmed trees. In the case of *G. palpalis* the author says "foreshore and river clearings will kill out *G. palpalis*." Symes and Vane [this *Bulletin*, 1937, v. 34, 542] have shown in Kenya that *G. palpalis* can be so reduced in numbers by the "block" method of catching as to make human occupation safe; this method is much cheaper than sheer clearing.

Small villages isolated in the great expanse of the tsetse-bush.—This situation has been dealt with by the Medical Department of Tanganyika Territory by forming settlements of people [this *Bulletin*, 1944, v. 41, 12].

Tsetse in and around towns.—During the years when farm land is lying fallow, the bush regenerates and a thicket suitable for *G. pallidipes* grows up ; this has occurred round Dar-es-Salaam and Tanga in Tanganyika Territory. *G. brevipalpis* and *G. austeni* commonly occur with *G. pallidipes* and are eliminated by the same measures. The thickets should be cut out, leaving the large trees.

Alienated land.—The measures to be adopted will depend on the local conditions ; cooperation by the owners of the land, advice by an expert, and supporting legislation will be required.

Two other methods of reclamation—organized grass fires and isolation of special vegetational areas by cleared barriers—may be mentioned but are not emphasized, the former is regarded as a subordinate measure to be used in certain conditions, while the latter needs very wide barriers, which are costly to maintain.

The prospect for large-scale reclamation.—Reclamation of areas of over 50 square miles can be successfully undertaken in some regions, *e.g.*, the great plains of the hard pan *Acacia-Commiphora* country. Cheap discriminative clearing has been recommended for an area of over 500 square miles at Arusha in Tanganyika Territory to free it from *G. swynnertoni* and *G. pallidipes*, while in the Musoma District of Tanganyika Territory there is a great island area of 300 square miles which has been surveyed and which, the author says, can undoubtedly be reclaimed cheaply from *G. swynnertoni*, *G. pallidipes* and *G. brevipalpis*. There are several thousand square miles of Tanganyika Territory which can be reclaimed at a cheap cost by methods already known to the Department. There remain enormous areas of " miombo " country infested by *G. morsitans*, great areas of thorn bush with *G. swynnertoni* and the vast *G. pallidipes* country.

The author gives a résumé of the large-scale experiments financed by the Colonial Development Fund which have been so seriously interfered with by the war. A combination of fire-exclusion and discriminative clearing of the hard pan in Shinyanga gave very good results, and a similar experiment has been made in Northern Rhodesia. Merely clearing a special type of valley in Northern Rhodesia, without fire-exclusion or organized burning, caused a large reduction in the number of *G. morsitans*.

The effect of " selective " clearing on *G. swynnertoni* is being tested, but results are not yet available. The author distinguishes between discriminative and selective clearing ; the former means the removal of a definite type of vegetation comprising different species, *e.g.*, hard pan clearing, while the latter refers to the removal of certain species of trees throughout the bush in whatsoever type of vegetation they may occur and results in the reduction of the vegetation to one or more species of trees left uncut.

An experiment with discriminative clearing of thicket to test the effect on *G. pallidipes* is being made at Shinyanga in an area of 3,700 acres of *Acacia-Commiphora* savanna. Other work is being done in *Isoberlinia-Brachystegia-Acacia-Combretum* savanna. In a small experiment by MOGGRIDGE at Kilifi, cutting out the undergrowth from 100 acres of coastal thicket greatly reduced the numbers of *G. pallidipes*.

Reclamation by shooting the game.—A large-scale game experiment was begun by the Tsetse Department but had to be closed down when war broke out. In Southern Rhodesia the shooting of game has been proved to be very effective, but the author states that it certainly cannot be applied everywhere owing to the topography of the country and the density of the bush; it may well play an important part in reclamation in East Africa.

Defence.—The cleared barrier of sufficient width is too difficult to maintain to be a practical measure except in special circumstances. Discriminative clearing, perhaps combined with fire-exclusion, may well provide the defence of the future and its study should be taken up again after the war.

The author thinks that the Diesel-engined caterpillar tractor should be very useful in places where population is sparse.

The international aspects of reclamation, the natural barriers like the Great Lakes, mountainous areas, great plains and cultivated areas are discussed, and the author concludes that, although in Tanganyika Territory the problem is much more difficult than in Southern Rhodesia, the successful operations in the latter territory are on such a large scale that they give confidence that improved methods of research will enable the Tanganyika problem to be tackled with equal success even in the southern part of the Territory. In the northern part, the Lake and Northern Provinces, he thinks that a complete survey would show that thousands of square miles could be reclaimed by present methods.

The author discusses certain other views which have been given from time to time, *e.g.* that sheer felling of vegetation, as required by the population, is sufficient; that tsetse flies are a blessing in disguise by protecting the soil from erosion. Finally, he refers to the organization necessary to carry out a tsetse policy and suggests the formation of a territorial tsetse committee composed of the Chief Secretary and the Directors of the Medical, Agricultural, Veterinary and Tsetse Departments; provincial sub-committees would also be formed. [In the abstracter's opinion this paper is a very important one, representing the views of a team of scientific workers who have closely studied the problems for many years.] *J. F. Corson.*

VAN HOOF, L., HENRARD, C. & PEEL, E. Recherches sur le comportement du "Trypanosoma gambiense" chez le porc. [**Behaviour of *T. gambiense* in the Domestic Pig.**] *Ann. Soc. Belge de Méd. Trop.* 1940. June 30, v. 20, No. 2, 203–26.

This paper is a reduplication of that abstracted in this *Bulletin*, 1943, v. 40, 367.

VAN HOOF, L., HENRARD, C. & PEEL, E. Irrégularités de la transmission du "Trypanosoma gambiense" par "G. palpalis." [**Irregularities in the Transmission of *T. gambiense* by *G. palpalis*.**] *Ann. Soc. Belge de Méd. Trop.* 1940, June 30, v. 20, No. 2, 227–43. [16 refs.]

This paper is a reduplication of that abstracted in this *Bulletin*, 1943, v. 40, 368.

MCCOMAS, G. & MARTIN, N. H. **Trypanosomiasis treated with Pentamidine: a Fatal Case.** *Lancet.* 1944, Mar. 11, 338–9.

The patient was an African soldier of the Gold Coast, West Africa, aged 28. He was admitted to hospital on February 26th, 1943, complaining of malaise and headache of three days' duration; on admission

he was observed to be somnolent. Trypanosomes were found in a blood film and his cerebrospinal fluid contained 170 leucocytes per cmm. He was given three injections [presumably intravenous] of 0·1 gm. of pentamidine—the first on March 10th, the second on March 11th, and the third on March 13th. After each of the first two injections he complained of pain in the left temporal region lasting for about two minutes; 10 minutes after the third injection he became unconscious and passed into status epilepticus. There was strabismus but his pupils were equal and reacted to light. Examination of the eyes on March 18th showed bilateral papilloedema. Soon after the fits began his temperature rose and remained between 102° and 105°F. until he died, on March 27th. His cerebrospinal fluid on March 18th contained 190 cells per cmm., 90 per cent. being lymphocytes, and 0·04 per cent. of protein; on March 25th it contained 230 cells and 0·06 per cent. protein. No trypanosomes were seen.

An autopsy was made within an hour after his death; sections of the brain showed widespread perivascular cuffing, conforming to MOTT'S description [*Rep. Sleeping Sickness Comm. Roy. Soc.*, No. 7, 1906]. The myocardium was apparently normal.

The authors think that the status epilepticus was caused by the drug, either by direct action on the central nervous system or from a Herxheimer reaction, the latter being more probable. [The somnolence on admission, the condition of the cerebrospinal fluid and the widespread perivascular cuffing suggest an infection of at least several months' duration. For other references to the use of pentamidine in human trypanosomiasis see this *Bulletin*, 1943, v. 40, 224, 370, 589; 1942, v. 39, 532.] *J. F. Corson.*

DENISON, Nadene. **Experimental Studies on *Trypanosoma cruzi* Infection and Reticulo-Endothelial Blockade in Rats.** *Amer. J. Hyg.* 1943, Sept., v. 38, No. 2, 178–84.

Since the intracellular stages of development of *T. cruzi* are located chiefly within the macrophages, experiments were conducted with the view of comparing experimental *T. cruzi* infection in rats with mechanical blocking of their reticulo-endothelial system by trypan blue. In addition to these, in another batch of animals the trypanosome infection was superimposed upon the R.E.S. block. In all cases the infection—produced by a culture (in NNN medium) of trypanosomes of the same strain—was transient, and the animals were kept under identical conditions.

It was found that the changes in body weight were slight and there was no significant difference among the three groups of animals as regards the percentage of body weight represented by the liver, spleen or heart. The differential blood counts showed a significant variation from the normal, which was similar in all the three groups of rats. The blood picture was characteristic of a chronic infection, with a slight leucopenia, moderate lymphocytosis and monocytosis. The blood serum of the infected animals was trypanolytic to cultures of *T. cruzi* in a dilution of one in five. In rats which were blocked as well, the time required to produce lysis was increased and the titre of the serum was reduced. *C. A. Hoare.*

Dios, R. L. & Bonacci, H. Sensibilidad de los sapos (Bufo arenarum) a la inoculación experimental del *Tripanosoma cruzi*. Segunda comunicación. [**Insusceptibility of the Toad** (*B. arenarum*) **to Infection with** *T. cruzi*.] *Rev. Inst. Bacteriológ. "Dr. Carlos G. Malbran."* Buenos Aires. 1943, Dec., v. 12, No. 1, 27–36, 2 folding pls. English summary.

"1. We inoculated experimentally 1,040 toads of the species *Bufo arenarum* with strains of *Trypanosoma cruzi* of diverse origins: human cases of natural and experimental infection (P.G.P.); naturally infected Triatoma infestans.

"2. We used 1,336 white mice and also 5 pups.

"3. The culture tubes used as checks amounted to 2,835 (culture media of Noguchi and Bonacci).

"4. Every toad inoculated with the different strains of *T. cruzi* remained negative. On the other hand, the sensitive animals and the cultures utilized as checks were constantly positive.

"5. These large scale experiments prove definitely that the toad (*B. arenarum*) is not susceptible to the experimental inoculation of *T. cruzi*."

Meyer, H. Culturas de tecido nervoso infectadas por Schizotripanum cruzi. [**Cultivation of** *T. cruzi* **from Infected Nervous Tissue.**] *Anais Acad. Brasileira de Ciencias*. Rio de Janeiro. 1942, Sept. 30, v. 14, No. 3, 253–6, 4 figs. on 2 pls. English summary.

"Cultures of brain and spinal ganglia of chicken embryos were infected with S. Cruzi. The nerve cells become infected like the other cells of the nerve tissue. Nerve cells support parasitism well up to the third day of infection. Thereafter, when the parasites are beginning to move, signs of structural desintegration are observed. The neurofibrillae are destroyed, the nerve fibre gives no further reaction with nitrate of silver. The nerve cell finally bursts and the new parasites are free to leave the cell."

LEISHMANIASIS.

Das Gupta, C. R. & Sen Gupta, P. C. **Agranulocytosis in Kala-Azar.** *Indian Med. Gaz.* 1943, Jan., v. 78, No. 1, 8–11, 5 figs. (1 coloured) on 2 pls. [10 refs.]

Though acute agranulocytosis as a complication of kala azar is of fairly frequent occurrence in North China, Huang having reported in 1942 that there had been 42 cases in a series of 554 proved cases of kala azar admitted to the hospital of the Peiping Union Medical College during a period of 10 years, the condition has rarely been reported from other kala azar areas. Thus amongst several thousand cases of kala azar treated during the same period at the Calcutta School of Tropical Medicine, no single case of this complication had been observed till the subject of the present paper was encountered. The patient was a Hindu female child 11 years of age. There had been a history of fever of four months' duration, and finally a four days' inability to swallow. Examination of the mouth showed a coated tongue, sore at the margins,

and congestion of the pharynx and tonsils. The cervical glands were enlarged. A blood count showed 750 white cells per cmm. with complete absence of neutrophils ; there were 600 lymphocytes, 7·5 plasma cells, 60 preplasmacytes and 82·5 large mononuclears. The aldehyde test being positive, a sternal puncture was carried out and leishmania demonstrated. In spite of treatment with pentnucleotide and intravenous glucose there was no improvement, death supervening a week after admission to hospital.

The bone marrow in this case conformed neither to agranulocytosis nor kala azar. In the latter condition in India, though the total nucleated-cell count differs little from that in normal persons, the proportion of white cells is below normal, owing to a decrease of the granulocytes, while there is an increase in the red-cell series. There is also an increase in plasma cells. In the present case the marrow was neither normal nor hyperplastic, but appeared to be definitely hypoplastic, the total nucleated cell count being only 16,000 per cmm. The increase in the lymphocyte and plasmacyte series was greater than in either of the diseases alone. In addition to the reduction in the granulocytes, there was also a reduction of the erythropoietic cells. It is concluded that the unusual character of the marrow was the result of the coexistence of the two pathological conditions, kala azar and agranulocytic angina. [See also this *Bulletin*, 1942, v. 39, 608.]

C. M. Wenyon.

BURKE, E. **Notes on the Control of Kala-Azar on Tea Estates.** *Indian Med. Gaz.* 1943, Jan., v. 78, No. 1, 20–26, 2 graphs.

The author writes of his 15 years' experience of the control of kala azar in two large tea districts in Assam (East Boroi and Mangaldai) The Mangaldai district, which is chiefly dealt with, has an area of about 150 square miles. In this area are 14 estates with a combined area of 9,708 acres and an average population of 26,000. One of the chief methods of control of kala azar is the early identification of every case, isolation and treatment of the patient, followed by a careful watch on contacts for the first signs of infection. During the latter half of the period of the author's service (1935–1942), 3,489 cases of kala azar were treated, 80 per cent. with neostibosan and the rest with urea-stibamine or solustibosan. Of the total, only 190 died of intercurrent infections or failure to respond to treatment. Constant mass surveys were carried out by inspections and general applications of the aldehyde test. Whenever cases were identified the patients were removed to hospital for treatment and the contacts thoroughly investigated. If a serious outbreak occurred, it might be necessary to burn the infected lines. Spraying of the habitations and of any surrounding uncleared bush, with a view to destroying the sandfly vector, was regularly undertaken. Cultivation of cleared areas is a potent method of sandfly control, so that establishment of gardens was always encouraged. New labourers were carefully examined before engagement, and certain castes, which experience had shown to be quite unsuitable for work on tea estates, were never employed. Care had to be taken that previously employed coolies suffering from kala azar did not return under an *alias*. The author's conclusion after his discussion, which is largely of local rather than of general interest, is that the policy he advocates has been successful in controlling kala azar in a crowded potential reservoir of infection, so that the disease has been kept down to the low average of 35·5 cases per annum.

C. M. Wenyon.

SACHDEVA, Y. V. **Treatment of Oriental Sore with Quinacrine.** *Indian Med. Gaz.* 1943, Jan., v. 78, No. 1, 19–20.

At the Mayo Hospital, Lahore, where oriental sore is fairly frequently encountered, the author has tried the atebrin infiltration treatment as recommended by FLARER [this *Bulletin*, 1939, v. 36, 454]. Atebrin not being available, quinacrine was employed in the treatment of 57 cases, in 55 of which leishmania were demonstrated.

For a single sore, 0·1 gm. in 1 cc. of distilled water was used, while for large sores or when several were present, 0·3 or 0·4 gm. in 3 or 4 cc. was used. The injections, which are somewhat painful, are made intradermally with a dental syringe in several places round the sore till it is completely infiltrated. To effect a cure, one treatment may be sufficient in some cases, but in others from two to five treatments at weekly intervals may be necessary. There is little pain after the injections, which are not followed by any inflammatory reaction. The treatment is especially useful for sores on the eyelids and lips, or other parts of the face where other forms of treatment are contraindicated. There is no scarring with non-ulcerating sores and only slight scarring with those in which ulceration has occurred. *C. M. Wenyon.*

KIKUTH, W. Quimioterapia de la leishmaniosis. [**Chemotherapy of Leishmaniasis.**] *Med. Colonial.* Madrid. 1943, Aug. 1, v. 2, No. 2, 101–13.

FEVERS OF THE TYPHUS GROUP.

DE LA LASTRA SOUBRIER, J. M. Las variantes " O " de las razas X de proteus en la reacción de Weil-Felix. [**Variability of the " O " Strains of *Proteus X* used in the Weil-Felix Reaction.**] *Med. Colonial.* Madrid. 1944, Jan. 1, v. 3, No. 1, 13–18.

The author has already shown that in plate cultures of O strains of *Proteus X19*, *Pr. XK*, and *Pr. X2* colonies are occasionally found which have the appearance and properties of H strains. He also showed that there are flagellar antigens which are common to *X19*, *XK*, and *X2*.

Even in non-motile O strains flagella can sometimes be demonstrated, and by a series of selective subcultures of such strains it is easy to obtain typical H colonies.

By continued subcultures for four months of *OX19*, *OXK*, and *OX2*, motile strains have been found to develop even though special selection of the colonies was omitted. The change to the H type was most pronounced in the case of *OXK*, and least pronounced in *OX19*. While this change was occurring some of the cultures retained their O characteristics of non-motility and a very slight tendency to the formation of flagellar antigens.

By careful selection of typical O colonies it is possible to maintain strains suitable for the Weil-Felix reaction. The cultures are best made on solid media incubated at 37°C. for 24 hours and then kept in the cold. The media should not contain carbohydrates fermentable by the organisms. The use of weak antiseptics such as phenol 1–1,000 for the inhibition of H colonies is not recommended.

The Weil-Felix reaction is much more reliable when perfectly pure O strains are used; with them the reaction to *OX2* is uniformly negative in typhus exanthematicus of the classical type, and false positives with *OX19* are much fewer.

Killed suspensions of O strains are quite suitable, but they must not be preserved in formol; phenol is suitable, and alcohol used in the customary way destroys the flagellar antigens. *John W. D. Megaw.*

PARK, J. H. & OFFENKRANTZ, F. M. **Immunologic Reactions following Typhus Vaccination in Army Personnel.** *J. Lab. & Clin. Med.* 1943, Dec., v. 28, No. 15, 1859–63.

The Weil-Felix test was carried out in four groups of persons in the South-West Pacific area. Their responses to *Proteus OX19* and *Pr. OXK* are summarised in the Table.

The "positives" group consisted of patients diagnosed as mite-borne scrub typhus; the "civilians" group was made up of 36 civilians who were natives of the area and 10 members of the Merchant Marine; the "officer-candidate" and "patients" groups were American personnel who had been vaccinated within the previous year with Cox's yolk-sac vaccine made from *Rickettsia prowazeki*. The "patients" were under treatment for malaria, syphilis, or dengue, the "officer candidates" were healthy.

Reactions to Proteus OX19 *and* Pr. OXK.

Titres to *OX19*	Positives	Civilians	Officer Cand.	Patients
0	12	44	124	254
1–10 to 1–20	15	2	22	25
1–40	7	0	0	0
1–80	1	0	0	0
1–160	1	0	0	0
Total	36	46	146	279
Titres to *OXK*				
0	0	36	22	72
1–10 to 1–20	0	9	116	178
1–40	0	1	8	23
1–80	0	0	0	6
1–160 to 1–1,280 ...	36	0	0	0
Total	36	46	146	279

In the "civilians" group the 10 who gave low-titre reactions with *OXK* including two who reacted 1–10 to *OX19*, were members of the Merchant Marine; all the 36 native civilians were completely negative to both organisms.

In the group of "positives" who were diagnosed as scrub typhus on clinical and serological grounds only one reacted to *OX19* at a titre of 1–160; his reaction to *OXK* was at the same titre.

The chief conclusions were; (1) Among persons vaccinated within the preceding 12 months (55 per cent. of these, about six months before the test) 88 per cent. were completely negative to *OX19*;

(2) it was perplexing to find that 80 per cent. of these persons reacted to *OXK*; (3) " Of the *OXK* reactions 86 per cent. were at a titre of 1–20; 1–10; or negative; from this we concluded that a titre of 1–40 was very suspicious and 1–80 diagnostic of scrub typhus." (4) The Rickettsiae used in making the vaccine were probably capable of inciting antibody response against *OXK*, and presumably of conferring some degree of immunity against scrub typhus.

The authors state that the term typhus, as generally used, refers to three groups of Rickettsial fevers: (1) louse-borne and flea-borne classical typhus; (2) tick-borne Rocky Mountain spotted fever; and (3) mite-borne scrub typhus and tsutsugamushi fever.

[The inclusion of the tick-borne and mite-borne fevers in the typhus group is a welcome sign that some workers from the U.S.A. are prepared to recognize the suitability of the name typhus for these two Rickettsial fevers and so to conform to the practice prevailing in other parts of the world. But flea-borne typhus is not generally regarded as classical typhus, and scrub typhus and tsutsugamushi fever are now considered to be the same disease.

The authors' findings are in some respects " perplexing " unless due allowance is made for variations in the agglutinability of different strains of the *Proteus* organisms and for the fact that the Weil-Felix reaction cannot be regarded as truly specific in spite of its great value in diagnosis.] *John W. D. Megaw.*

GAASE. Titerschwankungen der Proteus OX_{19}-Agglutination nach Weil-Felix. I. Beobachtungen von Titerschwankungen innerhalb von Tagen und Stunden bei Fleckfieberkranken und Rekonvaleszenten. [**Fluctuations in the Agglutination Titre of *Proteus OX19* in the Weil-Felix Reaction.**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1943, Aug. 10, v. 103, No. 4, 277–82, 29 figs.

The Weil-Felix reaction is recognized as being a non-specific antigen-antibody reaction which may remain positive for many years.

The Weil-Felix titre of 15 persons convalescent from typhus were observed at five-day intervals for several months. In 65 per cent. of these there were great fluctuations which, when shown as graphs, resembled the temperature curves of septic patients with deeply remittent or even intermittent types of fever.

So also 67 per cent. of the sera of 46 typhus patients, tested from the onset of the illness, showed even greater fluctuations in the titre instead of the gradual rise and steady fall that might have been expected.

In one extreme example the titre was 1–400 on the 4th day, it fell to about 1–20 on the 6th, and rose to 1–6, 400 on the 8th day. In another it was 0 on the 3rd day; 1–6,400 on the 8th; 1–200 on the 10th; and 1–12,800 on the 17th day.

The titre was usually, though not invariably, much higher after the nightly fast than two or three hours after a meal; sometimes a strongly positive reaction in a fasting patient became negative after food; the tendency of the titre to fall after food was most pronounced in convalescents.

Among the 160 mild and moderately severe cases studied in the investigation there were 9 (5·6 per cent.) who gave negative responses throughout the whole period.

The importance of making repeated tests in fasting patients is stressed. *John W. D. Megaw.*

MEYER, R. Ueber das Verhalten von Citochol und Meinicke bei Fleckfieberschutzgeimpften (Weiglscher Impfstoff). [**The Citochol and Meinicke Reactions in Persons Vaccinated with Weigl's Typhus Vaccine.**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1943, July 5, v. 103, No. 3, 161–4.

The author has already shown that the sera of typhus patients gave some response to the Citochol Test in 26·3 per cent. of the cases, and to the Meinicke K. R. II Test in 10·5 per cent. Only 4·5 per cent. of the sera gave responses with both of these tests; in 2·4 per cent. both reactions were doubtful (+ to ++) and in 2 per cent. there was a doubtful reaction to one of the tests and a definitely positive one (+++ to ++++) to the other. In none of the 712 sera tested was the reaction definitely positive to both tests [see this *Bulletin*, 1943, v. 40, 689].

In the present investigation 310 sera of persons inoculated from 5 days to 16 months previously were tested, and were compared with the responses in 385 control sera. The results were :—

	Inoculated	Controls
Doubtful positives to both tests ...	1·3 per cent.	6·3 per cent.
Doubtful positives Citochol only ...	16·4 ,,	15·6 ,,
Doubtful positives Meinicke only ...	5·8 ,,	6·5 ,,

The lapse of time after vaccination had no influence on the results.

It was concluded that vaccination by Weigl's method did not affect the responses to either of the reactions.

Doubtful reactions were considerably more numerous among troops in the East than in the West; climatic influences may have been responsible for this difference in the responses.

John W. D. Megaw.

BERRIO Y CAVA, E. D. Algunas consideraciones sobre el empleo y resultados de la vacuna del Dr. Blanc contra el tifus exantematico. [**Observations on the Results of Vaccination against Typhus with Blanc's Vaccine.**] *Med. Colonial.* Madrid. 1943, Aug. 1, v. 2, No. 2, 126–31.

In July 1941, 168 prisoners in Uad Lau in Spanish North Africa were vaccinated with Blanc's flea-faeces vaccine. Only seven had local and febrile reactions lasting three to five days. No case of typhus occurred in the prison till 14 months later when 100 of the vaccinated persons were still in the prison and there were also 200 unvaccinated persons.

Five of the vaccinated prisoners were attacked and two of them died: there were six attacks with one death among the other 200 who had not been vaccinated. It appeared, therefore, that any protective value had been lost within 14 months.

In October 1942 " before the outbreak had been controlled " 272 prisoners who still remained in the prison were vaccinated by the same method. Only three had local and febrile reactions. No further cases occurred although conditions were regarded as being still favourable for the spread of infection. It is stated, however, that other measures had been taken, including disinfestation and segregation of the sick,

and no mention is made of the dates of occurrence of the attacks prior to vaccination, so that the evidence of the protective influence of the vaccine is not very convincing.

The authors state that more than one and a half million persons have been vaccinated by this method in French North Africa.

John W. D. Megaw.

KRONTOVSKAYA, M. K. Uspekhi sovetskikh uchenykh v izuchenii rikketsiozov. [**Advances in Soviet Research on the Rickettsiases.**] *Zh. Mikrobiol.* Moscow. 1942, No. 11/12, 59–61. [Summary taken from *Vet. Bull.* 1944, Apr., v. 14, No. 4, 122. Signed A. MOLDAWSKY.]

This is a discussion on the development of Soviet research on rickettsiases. The chief work on epidemiology, histology of lesions, vaccination against *R. prowazeki*, and cultivation of the organism, is discussed.

There is also a short report on three rickettsial infections which have recently been recognized and investigated in the U.S.S.R.; one of these occurs on the Black Sea coast and is probably identical with Marseilles fever; the second was met with in the Far East, Central Siberia, and the Chabarovsk district and was identified as Malayan typhus, type W.; the third, occurring on the Caucasian Black Sea shore, was related to murine typhus.

MAILLARD, E. R. & HAZEN, E. L. **A Second Report on Rocky Mountain Spotted Fever in New York State exclusive of New York City.** *New York State J. of Med.* 1944, Jan. 1, v. 44, No. 1, 73–5. [13 refs.]

In 1935 the authors reported 10 cases of Rocky Mountain spotted fever from one County in Long Island. Since then 26 cases have been diagnosed in Long Island, which is the only known focus of the disease in New York State.

All the patients lived in rural areas; cases occurred in spring, summer and autumn. There was a history of tick bite or contact with ticks in 24 of the 26 cases, but not infrequently the site of the bite could not be detected. The symptoms corresponded with those of Rocky Mountain spotted fever as described by RUMREICH [this *Bulletin*, 1933, v. 30, 899] and PARKER [*ibid.*, 1938, v. 35, 800]. Most of the cases were mild, but there were six deaths.

The maximum agglutination titres were as shown in the table :—

Titre	1–160 or over	1–80 or under	Negative
Proteus OX19...	24	2	0
Pr. OX2	4	8	14
Pr. XK. (O–HO reversion) ...	0	0	26

In the first week the titres ranged from 0 to 1–80; "between the second and third week after onset" titres of 1–160 to 1–2,500 were

observed. The titre for *OX2* was higher than that for *OX19* in two of the cases ; in one of these the titre for *OX2* was 1–1,280, and for *OX19* 1–160, after two weeks of illness.

The *OX2* and *OXK* strains were obtained from the Lister Institute, and the *OX19* strain from Dr. MOOSER. Alcohol-treated suspensions were used.

The agglutination of *OX2* by some of the sera helped to differentiate Rocky Mountain spotted fever from endemic (flea-borne) typhus.

A total of 36 cases from Long Island has now been studied serologically since 1926, when presumably the disease was first recognized in that area. [See also this *Bulletin*, 1936, v. 33, 47.]

John W. D. Megaw.

YELLOW FEVER.

BUGHER, J. C., BOSHELL-MANRIQUE, J., ROCA-GARCIA, M. & OSORNO-MESA, E. **Epidemiology of Jungle Yellow Fever in Eastern Colombia.** *Amer. J. Hyg.* 1944, Jan., v. 39, No. 1, 16–51, 5 figs. & 3 maps. [21 refs.]

The discovery of jungle yellow fever near the foothills of the Andes in Eastern Colombia in 1934 stimulated the Colombian Government, in collaboration with the Rockefeller Foundation, to set up a field laboratory in the village of Restrepo. As cases continued to appear in the area it was decided to establish a well-equipped virus laboratory to serve as a centre for epidemiological and laboratory investigations. The town of Villavicencio was chosen as the site and a suitable building was erected. This laboratory began operations in March of 1938, and has steadily functioned since. The data reported in this paper represent the results of intensive studies for a period of two years ending in January 1942.

As a result of previous studies, techniques for animal and insect work had been elaborated, equipment designed and plans made for the transportation and setting up of mobile field laboratories on short notice. Fortunately, six favourable opportunities for field studies developed within reach of Villavicencio during the period covered by this report. The time of the investigation and the area were determined by the discovery of a human case of yellow fever, usually by the viscerotomy service. With a minimum of delay the field laboratory was set up at the probable site of infection of the known human case. In general, the programme involved the capture of all living things that could be found in the area. These were roughly classified and combined in groups with the preservation of material for subsequent identification. In the case of arthropods and other insect groups specimens were triturated in normal monkey-serum-saline and the suspensions centrifuged. This material was inoculated intracerebrally into mice and subcutaneously into rhesus monkeys in the hope of isolating virus. The animals captured were bled at once to determine the possibility of circulating virus or of circulating antibodies. At first, the investigations were made as comprehensive as possible, but as experience accumulated, attention was more and more confined to mosquitoes and to monkeys and marsupials.

In the course of these studies yellow fever virus was isolated 13 times from *Haemagogus capricorni* and once from *Aëdes leucocelaenus*. No virus was found in any other arthropod form. Transmission by bite to rhesus monkeys was obtained twice in groups of *Haemagogus capricorni* found infected in nature. Numerous monkeys of different species, and several species of marsupials, were found to have specific antibodies in their sera. Some of the marsupials developed their antibodies in the month after their capture, indicating that their infections had been acquired just prior to capture. Occasionally other animals were found to be immune, but it appears that genera other than primates and marsupials play little rôle in the epidemiology of yellow fever in this region. No virus was found in mosquito larvae collected in the study areas.

Since *Haemagogus* appeared to be of such importance in transmission of yellow fever, special attention was given to its study. *Haemagogus* is a forest mosquito. Comparatively little is known of its breeding habits. Larvae in nature are found almost entirely in tree holes. Adults have been found several hundred metres from the nearest known breeding places, indicating that under certain conditions fairly long flights may be made. This mosquito is outstandingly arboreal and, especially during the dry season, it may be found only in the tree tops. Here it may persist throughout the dry season, and infected mosquitoes may thus carry over virus into the next breeding season at the beginning of the rains.

On the basis of the information accumulated in this study the authors deduce the following explanation of the epidemiology of jungle yellow fever in Eastern Colombia. It is primarily a disease of jungle animals, the virus being transmitted from animal to animal by certain mosquitoes which are strictly forest inhabitants. The animal phase is exclusively mammalian, and for practical purposes is confined to the primates and the marsupials, both of which are arboreal. The multiplication of virus and its circulation in the blood are transitory and persist for a few days only. Antibodies are produced, leaving a permanently immune animal. The jungle virus does not appear to produce any important illness in the susceptible animals. Ordinary movements of such animals are therefore not seriously impeded and their migrations can play a definite part in the spread of the virus. On the introduction of virus into a region which has no immune animals, the outbreak may be explosive in character with the result that within a relatively short time nearly all the monkeys and opossums may be immunized, and the epidemic in the area dies out. Under such conditions, another outbreak cannot be expected for several years until a non-immune population is re-established. Where the susceptible animals multiply rapidly, the animal outbreak may tend to be prolonged. This is particularly true in areas where marsupials produce two large litters a year. If no severe dry season occurs, the virus may persist in such an environment over several rainy seasons, showing the characteristics of endemicity. Several other species of mosquitoes than *Haemagogus* may at times play some part in the transmission of yellow fever in this area. Among these are *Aëdes leucocelaenus*, *Aëdes fluviatilis* and *Aëdes scapularis*. Practically, the essential vector appears to be *Haemagogus capricorni*.

For the most part the human element in jungle yellow fever appears to be casual. It is particularly among the persons who disturb the

forest by clearing that the disease tends to occur. Where the human population is abundant, *Haemagogus* may act as a vector from man to man. *Hugh H. Smith.*

BUGHER, J. C. & SMITH, H. H. **Antigenicity of Yellow Fever Vaccine Virus (17D) following Fifty-Seven Subcultures in Homologous Immune Serum.** *Amer. J. Hyg.* 1944, Jan., v. 39, No. 1, 52–7.

The production of yellow fever vaccine (17D) was begun in the Laboratories of the Yellow Fever Service of Brazil in 1937 and during that year and in 1938 a highly successful campaign, judged both by the mouse protection test results and by the sharp reduction in the incidence of yellow fever, was carried out, in which over 500,000 persons were inoculated with the cultured virus. The vaccines used throughout this period were prepared with virus from the 229th to 255th passage in tissue culture. However, during the 1938–39 yellow fever season in southern Brazil, both epidemiological observations and the post-vaccination immunity survey showed serious failure of several lots of vaccine to protect. These lots were all prepared from relatively high subculture passages; that is, from the 305th to the 391st subcultures. Experimental work carried out in the Bogotá, Colombia, laboratories demonstrated that high subcultures did not in themselves necessarily produce a loss of immunizing efficiency [see this *Bulletin*, 1942, v. 39, 77]. The experimental lots of vaccine used in this study were from the 212th and the 450th subcultures, greatly exceeding the range which was suspected of having produced difficulties in Brazil. Attention was therefore turned to other factors.

Customarily, the 17D strain of virus is cultivated in a medium to which normal human serum has been added. The serum used is always a pool from donors whose sera have given clearly negative mouse protection tests. It has been shown that when human blood samples are taken in a yellow fever region an appreciable portion of the sera giving negative results, when tested by the routine intraperitoneal method, may be shown by a more sensitive test to contain weak, but specific, antibodies. Since the unsatisfactory lots of vaccine in Brazil were prepared from virus grown in cultures employing pools of human serum collected in a known yellow fever region, it was considered highly probable that the virus had multiplied in contact with specific yellow fever antibodies, and that this contact might have modified the virus strain so as to impair its antigenic value.

Beginning with material of the 236th subculture, parallel series of cultures were maintained for 57 passages. The technique was the same for both with the exception that in one series a constant amount of immune human serum was added to each culture. The same pool of immune serum was used throughout, sufficient to make 0·1 per cent. concentration in the medium. This was found to be the maximum concentration which would allow satisfactory multiplication of the virus. At the 294th subculture lots of vaccine were prepared from each series. These were tested in human groups for their ability to produce antibodies under as nearly identical conditions as possible.

Groups of approximately 20 men, whose sera had previously been shown to be free of demonstrable yellow fever antibodies, were inoculated with serial dilutions of both the experimental lots of vaccine. The groups receiving the largest doses of virus were given a calculated dose of 10,000 M.L.D. for mice; the next groups 1,000 M.L.D.; the

next 100 M.L.D. and the last groups 10 M.L.D. At the end of one month the men were bled a second time. Mouse protection tests on the sera showed no significant difference in the efficiency of immunization with the two lots of vaccine. There was little failure to immunize save in the last group, which received approximately 10 M.L.D. per person. These results are in agreement with previous conclusions that for satisfactory immunization of man by the 17D virus amounts equivalent to 100 M.L.D. for mice, or more, must be used. It thus appears that cultivation of yellow fever virus in the presence of antibody barely insufficient to prevent multiplication does not produce any modification with respect to antigenicity in man as measured by the intraperitoneal mouse protection test. *Hugh H. Smith.*

BUGHER, J. C. & GAST-GALVIS, A. **The Efficacy of Vaccination in the Prevention of Yellow Fever in Colombia.** *Amer. J. Hyg.* 1944, Jan., v. 39, No. 1, 58–66. [13 refs.]

Reported studies on the immunity produced in man by vaccination against yellow fever have, in general, been limited to the demonstration of neutralizing antibodies in the blood sera of vaccinated persons. This paper sets forth direct evidence of the absence of yellow fever in vaccinated persons whose exposure is manifested by the appearance of cases in others of the same community.

In the interval between the introduction of yellow fever virus into the Rockefeller Foundation laboratories in 1927 and the first successful attempts to immunize investigators in 1931, a total of 16 cases of yellow fever, five of them fatal, occurred among 55 laboratory workers exposed to the virus. Since vaccination became available in 1931 not a single case of yellow fever infection has been encountered in over 200 such persons, even though some of the workers are known to have been bitten by infected mosquitoes in the field, and in several instances accidental inoculations of virulent yellow fever virus have been reported.

Beginning in 1937, a large scale vaccination campaign was undertaken in Colombia to protect the population against yellow fever in regions where conditions appeared favourable for the existence of the disease. At the end of 1942 a total of 605,781 individuals had received the vaccine. Careful records were kept of those inoculated, so that subsequently individuals could be definitely identified. Of the 198 proved and 45 probable cases of yellow fever which were discovered in Colombia after the initiation of the vaccination campaign only one occurred in a person who had received vaccine. This was in a boy inoculated five days before he became ill, when he was apparently in the incubation stage of the disease and before the production of antibodies could be expected. Many of these cases occurred in known endemic areas where over 90 per cent. of the population were vaccinated. Yellow fever continued in the small unvaccinated fraction while it disappeared among those inoculated. It is generally recognized by the people themselves in the endemic areas that a person who is vaccinated against yellow fever will not develop the disease.

In Muzo, a notorious area of yellow fever endemicity, 61 per cent. of the people had been vaccinated by the end of 1938. During both 1941 and 1942 cases of yellow fever were discovered in Muzo. In spite of the fact that the non-vaccinated part of the population was diminishing,

the cases occurred exclusively in this minority. The experience here indicates that the immunity following vaccination was effective for at least four years.

Of the 7,003 post-vaccination sera collected in Colombia, and tested by the intraperitoneal mouse protection test, only 6·6 per cent. failed to show evidence of protective antibodies. It could be expected that some cases of yellow fever might have been found among those giving negative protection tests. Such a result has not been encountered. This would indicate that, under natural conditions of infection, the actual degree of immunity conferred by the vaccination is appreciably higher than would appear from the protection test results. However, in practice, it is felt that such non-reactors should be revaccinated.

Hugh H. Smith.

BEVIER, G. **Some International Aspects of Yellow Fever Control.** *British Guiana Med. Ann. 1943.* 13–31, 1 map. [26 refs.]

The epidemiology of yellow fever both in the jungle and in towns and cities is briefly discussed and the appropriate measures of control are outlined. The necessity for international co-operation in the investigation of yellow fever and in the application of measures to prevent its spread to uninfected areas is emphasized. The author makes a plea for some recognition for those countries which have studied their yellow fever problem and have rendered their cities and ports free from *Aëdes aegypti*. He suggests the following classification of areas in regard to yellow fever : (1) Infected areas, where clinically recognizable *Aëdes aegypti*-transmitted cases exist. (2) Endemic areas, where the existence of jungle yellow fever is suggested by positive protection tests in children under six years of age, or demonstrated by viscerotomy, or where jungle yellow fever is suspected, but where adequate studies have not been made ; or urban areas which have traffic with such forest areas and do not attempt to control *Aëdes aegypti*. (3) Potential epidemic areas, wherever *Aëdes aegypti* mosquitoes occur. (4) Sanitary areas, in which ports and airfields and areas about them are free af *Aëdes aegypti*. *Hugh H. Smith.*

POTENZA, L. La viscerotomia en Venezuela. [**Viscerotomy in Venezuela.**] *Rev. Sanidad y Asistencia Social.* Caracas. 1941, Aug., v. 6, No. 4, 461–8. English summary.

In 679 viscerotomy specimens examined in Venezuela from 1937 to 1940, no evidence of yellow fever was found. Certain suspected cases were found to be due to poisoning by carbon tetrachloride.

Charles Wilcocks.

SÁ ANTUNES, W. S. O Serviço Nacional de Febre Amarela e suas realizações. [**The National Yellow Fever Service of Brazil.**] *Hospital.* Rio de Janeiro. 1943, Jan., v. 23, No. 1, 5–18, 9 figs. (3 maps).

PLAGUE.

TOWNSEND, S. L. **Plague (Bubonic and Pneumonic) in Port Said.** *J. Roy. Nav. Med. Serv.* 1944, Jan., v. 30, No. 1, 25–9.

Port Said, at the entrance of the Suez Canal, and a universal port of call for shipping from all parts of the world, reports cases of human plague every year. Plague is therefore endemic here and might possibly become epidemic. Only one case was recorded in 1940; in 1941 there were 12, and in 1942 six cases. As often happens, diagnosis of first cases may be delayed and it is only with the declaration of plague infection that an expectant look-out is developed. Bacteriological diagnosis, which is easily obtained by examination of the material from aspiration of the bubo, confirmed the clinical verdict. A useful feature clinically is the extreme tenderness of the bubo: even when the patient is semi-conscious he will stir when it is touched.

Treatment of cases in 1941 was by M. & B. 693 in the high dosage of 12 gm. orally on the first and second days, and 6 gm. on the third and fourth days. Apparently there was little effect in the small number of cases treated on either the prognosis or the clinical course of the disease. Prophylactic measures were of the usual type, including vaccination of the entire Arab population. Restriction of movement generally was impossible as otherwise the work of the port would have been brought to a standstill. In 1942, however, a much more frightening event occurred, namely, the outbreak, after the usual bubonic cases, of pneumonic plague. It was the first time that pneumonic plague had occurred in Port Said. Once more the intimation of the fact was delayed and the first diagnosis was "pyrexia of unknown origin" and terminal bronchopneumonia. By the seventh day the first patient was coughing up blood-stained fluid, and three days later his three brothers became ill, all on the same day. Altogether there were nine cases of this septicaemic or pneumonic plague. Clinically the cases resembled severe bronchopneumonia and the blood-stained sputum contained numerous plague bacilli. Treatment by sulphapyridine (2 gm. every four hours) and 40 cc. antiplague serum daily for three days do not seem to have influenced the lethal outcome. This pneumonic epidemic of nine cases seems to have lasted for about a month and then ceased. "Preventively the civilian authorities were loath to take drastic measures but the Services . . . cut down communication between the civilian and Service personnel in the town to a minimum."

W. F. Harvey.

METZNER, S. Entwicklung und gegenwärtiger Stand der Pestverbreitung in Afrika. [**Development and Spread of Plague in Africa.**] *Deut. Tropenmed. Ztschr.* 1943, Aug. 1 & Sept. 1, v. 47, Nos. 15/16 & 17/18, 399–423; 465–78. [Numerous refs.]

This publication is an abbreviation of a doctorate thesis presented at Hamburg in 1942. It gives a fairly complete review of the present position of plague in the African continent. The subject is treated regionally under the five headings, North Africa, West Africa, South Africa, East Africa and Madagascar. In his account of North Africa and Egypt the author refers to the pandemic of plague which broke out in Egypt in 1899. It was not in that year, however, but in 1869 that the Suez Canal was opened. His summary, which omits all the statistical data given in the text, is as follows:—"Although the

epidemiology of plague was cleared up at the beginning of the last pandemic and counter measures had been instituted everywhere, the disease has established itself in large areas of Africa. The classical measures (isolation, destruction of rats, inoculation) have failed against these secondary enzootic foci among the wild rodent population. Plague authorities are confronted with new and difficult tasks. The territories which are pest-ridden in this sense are mainly South Africa and certain parts of North and West Africa, while in East Africa and Madagascar the chief danger is from the house rat and its fleas. Deratization, protective inoculation and creation of rodent-free zones are the most effective anti-plague measures against the so-called sylvatic plague. In this connexion reference may be made to the new vaccine developed in the Pasteur Institute of Tananarivo." *W. F. Harvey.*

TRUFANT, S. A. **Sylvatic Plague: Probable Origin in United States, Distribution, Potentialities as Reservoir for Infections in Man.** *New Orleans Med. & Surg. J.* 1943, Nov., v. 96, 184. [Summary taken from *J. Amer. Med. Ass.* 1944, Jan. 29, v. 124, No. 5, 325–6.]

Trufant presents a historical review of plague in the United States. According to the importation theory, infected rats carried the plague in ships from the Orient to San Francisco. The enzootic theory suggests that plague infection is enzootic in the Western United States, as it is in Asia and probably the steppes of Russia and in South Africa. Plague in wild rodents exists in at least twelve of the Western states. Localized epizootics occur usually in the early spring. A vector is substantially indispensable to complete the propagation of plague among wild rodents. For the ground squirrel the vector is the flea Diamanus montanus. This flea not only harbored Pasteurella pestis but also conveyed it from squirrel to squirrel. These fleas are known to be capable of transmission of the infection after several months of "storage" and starvation. Very low temperature seems to increase the period of infectivity. So far spontaneous infections or reservoirs of plague have been established in over 31 rodents and in rabbits, the former including ground squirrels, marmots, chipmunks, wood rats, kangaroo rats and prairie dogs. Plague once established in a wild rodent population persists, but what the mechanism is has not been demonstrated. The author presents tables which list infected rodents and arthropods and the states in which they were found. Sylvatic plague as transferred to man in the United States was not pneumonic or extremely virulent. However, it is at least theoretically possible that plague might appear in epidemic proportions provided certain conditions as yet inadequately understood are conducive to an increased distribution of the infective agent.

SÁENZ VERA, C. Campaña antipestosa intensiva en la provincia del Chimborazo (Ecuador). [**Intensive Anti-plague Measures in Chimborazo (Ecuador).**] *Bol. Oficina Sanitaria Panamericana.* 1943, Oct., v. 22, No. 10, 873–82, 1 fig. (map). English summary.

In this anti-plague campaign the province of Chimborazo was divided into three parts, served by three brigades, each consisting of a chief inspector, inspectors and workers. The work was synchronized throughout the province so that no overlapping took place.

According to MACCHIAVELLO [this *Bulletin*, 1941, v. 38, 624], working in Brazil, fleas inhabiting the nests of rats can preserve a plague infection for a long time so that the conditions required for its emergence in epizootic or epidemic may be maintained. His conclusions have been confirmed and they represent an important consideration for antiplague measures on a large scale. They also account for the absence of plague during certain months of the year (July to December) in Chimborazo. Another point made is that guineapigs, or cuis, are often responsible for epizootics and that here these rodents are describable more as domestic than sylvatic.

Many nests and burrows of rats were destroyed by the use of cyanogas and flame-throwing bombs. Results seem to have been eminently satisfactory. A paste of arsenic and phosphorus was used in the burrows. Cuis (guineapigs) are beset with fleas, mostly of the species *Rhopalopsylla clavicola* along with a small percentage of *Pulex irritans*. Migration of rodents to a distance is not considered to be a factor in the spread of epizootics. There is too much food obtainable in any district; one result of this rodent localization is the strict limitation of outbreaks of human plague, in many cases to a single family.

In Chimborazo there were 82 cases of plague in 1939, 40 in 1940, 39 in 1941, 1 in 1942, and none in the first half of 1943. During the period August 1st, 1942, to July 31st, 1943, 43,867 rats were trapped (13,730 *R. rattus*; 10,322 *alexandrinus*; 19,815 *musculus*) and the spleens of 23,629 rats were examined at the Riobamba laboratory with, however, only one positive (species *rattus*). The campaign during this period is shown to have been successful in terms of rat extermination and reduction of human plague. *W. F. Harvey.*

PORGES, R. **The Use of Curtain Walls in Ratproofing.** *Pub. Health Rep.* Wash. 1943, Dec. 24, v. 58, No. 52, 1881–5. [10 refs.]

Curtain walls are non-weight-supporting and are placed in the ground outside buildings which require to be protected against the ingress or egress of rats. Such walls are needed where foundation walls are of insufficient depth: experiments have been instituted to determine the depth to which rats will burrow. If the test rats are well fed, the limit found was approximately 22 inches, but that this was not a safe limit was demonstrated by the typhus control programme at Charleston S.C. Protection by curtain walls is specially needed for food establishments. Rats were found to be able to burrow even under 48-inch curtain walls, but the addition of a 12-inch horizontal flange at the base of the wall defeated the rat completely. "A concrete L-shaped wall was developed consisting of a vertical portion approximately four inches thick, having a horizontal flange at the bottom two inches thick extending eight inches out from the vertical or 12 inches over-all horizontal measurement." As regards depth, a "24-inch L wall protected all units, including 10 food establishments." "While rat-proofing old buildings, many foundations are encountered extending 18 to 24 inches below ground surface that may be protected by merely installing a flange at the base." If the establishments already have concrete floors, it is doubtful whether curtain walls are necessary. *W. F. Harvey.*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

BRINK, V. **Amoebiasis.** *South African Med. J.* 1943, Dec. 11, v. 17, No. 23, 363–6. [19 refs.]

The importance of amoebiasis is not sufficiently appreciated in the Army; in civil life amoebiasis causes much illness of which the true cause is frequently not suspected, and in military life exposure to infection is greater. Amoebiasis is not confined to the tropics, it is widespread throughout the world. In the United States 5–10 per cent. of the population are infected; in New Guinea over half the inhabitants have positive stools; in South Africa infection must be at least as common as in the United States, especially in the warmer zones such as Natal.

The symptoms of amoebiasis are exceedingly varied, and may not necessarily be referred to the abdomen. In 100 consecutive cases seen by the author the diagnoses, on admission to hospital, included anaemia (2), malaria (1), pneumonia (2), pleurisy and influenza (2), haemorrhoids (2), and peptic ulcer (3). He classifies the cases clinically as follows:—

Group 1.—Chronic amoebic neurasthenia, fairly common and easily overlooked.

Group 2.—Chronic intermittent amoebiasis, with periodic diarrhoea. Some of these patients may become chronically constipated, others may become anaemic, without much abdominal trouble. Pain in the abdomen may be a feature, and may be colicky, generalized or localized, leading to operation for appendicitis. Irregular pyrexia and headache may be features of chronic intermittent amoebiasis.

Group 3.—Chronic progressive amoebiasis. In this group are included patients with chronic dysenteric amoebiasis, ulcerative colitis or liver abscess.

Group 4.—Dysenteric amoebiasis. In this group are included those with true acute amoebic dysentery which, except in the tropics, is relatively uncommon.

Group 5.—Latent amoebiasis, the subjects of which present no symptoms; they are the "carriers," or "cyst passers." The author argues that patients suffering from acute amoebic dysentery, and passing active amoebae in bloody stools, are not really infective to others, since ingestion of these active forms cannot give rise to new infection. Infection has been shown to occur only when cysts are swallowed, and the real danger to the community, therefore, is the apparently healthy person in whose faeces cysts are present. He develops the view that all persons harbouring *Entamoeba histolytica* should receive treatment, whether the infection causes symptoms or not.

Emetine alone cannot be relied upon to cure amoebiasis, though it is often effective in causing disappearance of symptoms, and, therefore, has a useful place in therapy. Emetine has a cumulative action which must always be remembered. The treatment advocated by the author is as follows:—

Patient confined to bed (14–21 days).—Daily emetine injections ($\frac{1}{2}$–1 grain) to a total of 10–12 grains, together with a suitable arsenical (carbarsone four grains twice daily for a week and repeated after an interval of four days) and daily bowel washes with 2 per cent. sod. bicarb. solution followed by retention enemata of 8 oz. Chiniofon

(Yatren), 2 per cent., for four days, then on alternate days, increasing the concentration to 5 per cent. These measures are used concurrently.

Patient convalescent.—An oxyquinoline derivative (Chiniofon, Yatren, Enteroviofoform, Diodoquin) by mouth for three days, followed by Kurchi—bismuth-iodide tablets, five grains twice daily for three days. These two measures are used alternatively (neither being given on the seventh day) for three weeks. *Charles Wilcocks.*

OSBURN, H. S. **Amoebiasis on the Witwatersrand.** *South African Med. J.* 1943, Dec. 11, v. 17, No. 23, 361–2.

Inhabitants of the Witwatersrand are exposed to two potential sources of amoebic infection, the first from African food handlers recruited from the endemic areas of Natal, Nyasaland, etc., the second during holidays spent in these areas. The author reports the result of stool examination of 60 Europeans and three Africans; many of these complained of abdominal trouble:—

E. histolytica trophozoites	1
E. histolytica cysts	5 (3 European, 2 African)
E. coli cysts	13
Iodamoeba bütschlii cysts	2
Endolimax nana cysts	1
Giardia intestinalis	2
Chilomastix mesnili	2

None of the three Europeans with *E. histolytica* cysts gave a history of dysentery; one was a chef on the railways.

Charles Wilcocks.

MUNK, J. **X Ray Appearances in Amoebic Hepatitis.** *Brit. J. Radiology.* 1944, Feb., v. 17, No. 194, 48–53, 8 figs. [10 refs.]

The direct radiological signs of amoebic hepatitis are limited. A Bucky film of the liver area may indicate its size and the portion enlarged. Sometimes gas may be visualized in an abscess cavity, thus affording an indication of its size and site. X-ray evidence of amoebic hepatitis is limited mainly to indirect signs on the right half of the diaphragm and to the right lower lung field, but only in upward enlargement of the liver can diaphragmatic changes be seen. This may be part of a generalized enlargement, or only the subphrenic part of the liver may be involved.

In the first group no radiological signs in the diaphragm can be expected, if the lower anterior part of the liver only is involved, or in intrahepatic or subhepatic abscess without generalized liver enlargement. Thus in most cases of evident enlargement of the anterior or lower part of the liver a diaphragm normal in position, shape and movement, can be seen on screening.

The second group is characterized by different degrees of elevation of the right half of the diaphragm, as part of a generalized enlargement, or due to localized subphrenic enlargement with degrees of restricted or abnormal movement and pathological changes in the right lower lung field. These points are discussed in a survey of 10 cases and are classified as follows:—

Elevation of the Diaphragm.

Total elevation.—The first seven cases showed different degrees of general elevation of the right hemi-diaphragm, in connexion with abnormal movement, blurring and a small pleural effusion, affording a clear radiological picture suggesting suprahepatic abscess.

Bulging of diaphragm.—Three belonging to the second group showed different degrees of bulging of the diaphragm with generally restricted movement, or absence of movement of the bulge on respiration, but normal, or even increased, excursion in the other part of the diaphragm.

Shape of the diaphragm.—The diaphragm either preserves its normal shape or the bulge into the chest increases. Two factors are responsible:—(1) increased intra-abdominal pressure, and (2) negative pressure within the thorax acting on a weakened diaphragm, when the costophrenic angle is narrowed. In one instance, however, this angle was increased from flattening of the diaphragm.

Movement of the diaphragm.—All degrees of restricted movement are found. It may be the only sign of a pathological liver condition. In the present series, with one exception, excursion was seen on respiration.

Finally the *value of paradoxical movement* of the diaphragm is discussed. This is elicited by Müller's and Hitzenberger's tests. The former—upward movement of the diaphragm on attempted respiration with closed glottis or nose and mouth—indicates damage to the power of contractibility of the diaphragmatic muscle. The latter test, produced by short inspiration through the nose with mouth closed, is a modification of the former. This causes a short lasting negative intra-alveolar pressure due to inspiratory expansion of the thorax with insufficient exchange of air. Only a diaphragm with normal contractive power is able to resist this lung suction caused by negative pressure and therefore moves normally; but a diaphragm, the contractibility of whose muscles is either impaired or lost, will follow suction of the lung and move *paradoxically* upwards on inspiration.

In the slowly working Müller's test, even a weakened diaphragm may be able to resist suction of negative intra-alveolar pressure and move normally, but on *sniffing*, with sudden onset of suction, only a diaphragm with normal muscles will move normally. Müller's and Hitzenberger's tests are positive in cases of paresis, or paralysis, of the diaphragm from injury to the phrenic nerve, anterior horn cells, or local damage.

In amoebic hepatitis (in three out of the series) paradoxical movement was attributable to the last-named condition. Blurring of the diaphragm (in two cases) was probably due to local changes and oedema.

Atelectasis of the right lower lung field.—Insufficient respiration of the lung field may be due either to direct pressure of the elevated diaphragm, or to partial or total restriction of movement of the right hemi-diaphragm; it is held responsible for insufficient ventilation and expectoration, which permits mucus to collect and block bigger or smaller bronchi, thus causing different degrees of atelectasis. These appear as small atelectatic zones of "plate-like" or "band-like" shadows in the lower lung lobes. At first the atelectasis is conical in shape and surrounds the involved bronchus, but soon it assumes a horizontal plate-like aspect because collapse can only occur in the cranio-caudal direction.

It can be assumed that many cases diagnosed as pneumonic consolidation are in fact atelectasis. *P. Manson-Bahr.*

DeLanney, L. A. & Beahm, E. H. **Balantidium Coli. Report of Case with Proctoscopic Study.** *J. Amer. Med. Ass.* 1943, Oct. 30, v. 123, No. 9, 549–50, 3 figs.

The patient, a man 33 years of age, gave a history of 17 years of repeated attacks of diarrhoea with passage of blood and mucus. At one time a diagnosis of *E. histolytica* infection was made, and emetine treatment instituted. As this drug was not tolerated, acetarsone was substituted. This controlled the condition for some weeks, but relapse occurred. The same result followed a second course of acetarsone. Finally, sigmoidoscopic examination was made. This revealed a diffuse inflammation of the rectal mucosa with irregular patches, resembling diphtheritic infection, in the upper part. When these patches were scraped off, microscopic examination of the material revealed numerous *Balantidium coli*. Treatment with carbarsone and then oil of chemopodium gave only temporary relief. Finally, diodoquin [di-iodohydroxylquinoline] was prescribed, ten 0·25 gm. tablets a day for 20 days. The patient improved and showed no sign of relapse for 18 months. Repeated examinations during this period failed to reveal any parasites. *C. M. Wenyon.*

Demianov, E. A. [**Ciliate of the Genus *Colpoda* found in a Child suffering from Haemorrhagic Colitis.**] *Med. Parasit. & Parasitic Dis.* Moscow, 1943, v. 12, No. 2, 60–64, 2 figs. [In Russian.]

In the course of investigations on intestinal diseases, carried out at Derbent (Caucasus) in 1937, the author on one occasion took a sample of faeces, with a sterile glass tube, directly from the rectum of a child aged 1 year 3 months, who had been suffering for some time from persistent diarrhoea. The faeces were fluid, with an admixture of mucus and pus. Part of the faecal specimen was examined in smears, while some of it was cultivated in Endo and John's [?] medium. After 24 hours at 37°C. there appeared in the latter a culture of ciliates belonging to the genus *Colpoda*. The ciliate was maintained for a year in this and other media, at 37°C. The detailed description, with illustrations, supports the author's diagnosis of the ciliate. [Though the author himself makes no inferences from his finding, there can be no doubt that this ciliate is not a human parasite, but represents a free-living coprozoic form, in the present case a "gut-passer" (*Darmpassant*). It had evidently passed through the alimentary tract of the child in the form of cysts, which hatched only when transferred to a suitable external medium.] *C. A. Hoare.*

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

Elsdon-Dew, R. **Relapsing Fever and *B. proteus X Kingsbury*.** [Correspondence.] *Nature.* 1943, Nov. 13, 565.

It was noticed in Ethiopia that there was an association between the finding of spirochaetes of relapsing fever in the blood and agglutination of *Proteus XK*. Of 650 cases in which spirochaetes were found, 211 gave agglutination of *XK* in dilutions of 1–100 or more, but no such level was found in specimens of serum sent for the Kahn test.

Agglutination tests with *Proteus XK* were made every fourth day in 110 patients positive for spirochaetes, most of whom were under arsenical treatment ; the results were as follows :—

Clinical course	Agglutination of *Proteus XK*, 1–100	
	Positive	Negative
No relapse	6	35
One or more relapses	22	27
Deaths...	—	20

In relapsing cases which responded there was a progressive rise in titre ; after the last relapse the titre fell rapidly, to less than 1–50 in a month.

These cases occurred in the highlands, where *Ornithodorus* is unknown ; the disease was probably louse-borne. Further investigation was not possible. *Charles Wilcocks.*

MARQUES, A. Febre recorrente de carraças atipica em Xinavane (Mocambique). [**Atypical Relapsing Fever in Xinavane (Mozambique).**] *An. Inst. Med. Trop.* Lisbon. 1943, Dec., v. 1, No. 1, 187–97, 2 folding graphs.

The relapsing fever in this district is transmitted by *Ornithodorus* [the species is not mentioned]. The incubation period ranges from "less than one week to more than two." The course of the fever is peculiar ; in some cases it is continued for a month and resembles that of typhoid fever ; but this, it is acknowledged, may be due to associated bronchopneumonia or nephritis ; in others, there may be pyrexia for some hours followed by an apyrexial period lasting for weeks, during which the patient may leave hospital and relapse after arrival home. Splenomegaly may be transient and even in severe cases may be absent ; it was not found in 18 per cent. of the author's patients. Nervous manifestations—neuralgia, neuritis, sciatica, epileptiform seizures—were common, as were ocular conditions, iritis, cyclitis, choroiditis, pneumonia and bronchopneumonia, serious haemorrhages, and oedema with albuminuria due to renal or cardiovascular lesions.

The disease is more resistant to arsenical treatment than is the ordinary type of relapsing fever. One patient, after a course of injections of 914 spread over five months, in a few days showed numerous spirochaetes in his blood. Bayer 205, Bismarsen and mercurials gave no better results. *H. Harold Scott.*

STAVISKY, J. D. [**The Treatment of the Middle-Asia Tick-borne Spirochaetosis with Myoarsenol.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1943, v. 12, No. 2, 56–9. [In Russian.]

The author reports the results of treatment of tick-borne relapsing fever in Middle Asia with a Russian drug produced in 1935 under the name "Myoarsenol," which contains from 18·5 to 19·5 per cent. arsenic. "Myoarsenol" is dissolved in 2–3 cc. distilled water at room temperature and is injected intramuscularly (into the buttocks) using a long

needle (5–7 cm.). The course of treatment is as follows: 1st day 0·15 cc., 2nd day 0·3 cc., 3rd day missed, 4th day 0·45 cc., 5th and 6th days missed, 7th day 0·45–0·6 cc.

The total number of patients treated up to the present is 40. As a rule the paroxysms of fever ceased by the 3rd day of treatment, after which no spirochaetes could be detected in the blood. There were no signs of arsenic poisoning and only two cases relapsed. The author regards the results as promising. *C. A. Hoare.*

ASHBURN, L. L. & PACKCHANIAN, A. **Histogenesis of Experimental Icterohemorrhagic Spirochetosis in Albino American Deer Mice** (*Peromyscus maniculatus gambelii*). *Amer. J. Trop. Med.* 1943, Nov., v. 23, No. 6, 607–13.

A study of the histogenesis of icterohaemorrhagic spirochaetosis in albino American Deer Mice, based on the study of 30 of these mice inoculated intraperitoneally with the D.C. (District of Colombia) rat strain of *Leptospira icterohaemorrhagiae*, and killed in groups at daily intervals from the 2nd to the 7th day.

Jaundice, internal haemorrhage, and leptospirae in the blood were first noted on the 5th day. Jaundice and haemorrhage rapidly increased and were marked by the 7th day. Leptospirae were present in the blood in great numbers by the 6th day but had decreased by the 7th day.

The kidney cortex, mainly the inner portion, showed progressive changes in the tubular epithelium, including cytoplasmic swelling, dispersion of granules, nuclear enlargement, and, in late stages, lack of adhesion between cells, and focal necrosis.

The pathological changes in the liver comprised cell enlargement, increase in number of nuclei in cells, swelling and oxyphilia of the Kupffer cells, necrosis of an occasional parenchymatous cell, and disruption of the liver cords. Erythrophagia was present on and after the 5th day and in the spleen was often prominent. Leptospirae were abundant in the liver, much less numerous in the kidney, and were present only in very small numbers in the heart and lungs.

The hepatic damage is considered sufficient to explain the occurrence of jaundice in these infected deer mice. Intra-hepatic biliary obstruction was not observed. *E. Hindle.*

YAWS AND SYPHILIS.

KALZ, F. & NEWTON, B. L. **Syphilitic Juxta-Articular Nodules.** *Arch. Dermat. & Syph.* 1943, Dec., v. 48, No. 6, 626–34, 3 figs. [34 refs.]

Juxta-articular nodes, first described fully by JEANSELME in 1899, are defined by the authors of the present article as painless, slowly growing subcutaneous fibrous nodules, often symmetrical in their distribution, and, if untreated, of long duration. They are situated in the vicinity of joints, especially of the extremities, and are not attached to the skin or related to bursae or tendons. According to Jeanselme, their sites of predilection are, in order of frequency, elbows, knees, tibial tubercles, sacrococcygeal area, and costal cage. Histologically, according to

Jeanselme, they show three zones, an outer one of monocellular cell exudate, with dilated blood channels in a loose connective tissue ; an intermediate, fibroma-like scar or tissue zone ; and an inner one of hyalinized tissue with amorphous changes. These changes were essentially those found in one of the nodes described by the present authors, with the exception that in their case there were cyst-like spaces bounded by fibre-like whitish to yellowish green tissue. Smaller nodules are fibroma-like.

The authors say that such nodes were described in 1778 by BERTIN as occurring in natives of Guadaloupe afflicted with syphilis and yaws. Other causes have been mentioned, *e.g.*, rheumatism by BARLOW, but whether or not such other causes are ever responsible, there can be no doubt about the frequency with which yaws and syphilis are present in such cases ; they occur more particularly in tropical and subtropical countries than in colder ones. Amongst other authorities quoted by the authors of the present article are HU and FRAZIER [this *Bulletin*, 1934, v. 31, 275], who found many such cases in China ; FENNER, similarly in the aborigines of Australia ; and HUDSON who found them as commonly in Euphrates Arabs suffering from bejel or non-venereal syphilis [*Bulletin of Hygiene*, 1936, v. 11, 908] as in areas where yaws was prevalent. JESSNER [this *Bulletin*, 1925, v. 22, 241], after studying syphilis in Siberia, as a member of the Russo-German expedition,

Fig. 1.—*A*, juxta-articular nodule of thirty years' duration on the left elbow, and one of fourteen years' duration on the right elbow, of a syphilitic Negro. *B*, juxta-articular nodule of thirty-five years' duration on the left knee of the same Negro.

[Reproduced from the *Archives of Dermatology and Syphilology*.]

declared that there was no way of differentiating such nodes occurring in syphilis from those in yaws.

The authors of the present article describe in detail a case of the kind in a 71-year-old negro who had suffered from untreated syphilis for probably over 35 years and had developed the first nodes, on the right and then the left knee, about a year after the first sore on his penis. He had subsequently developed nodes on the elbows, as shown in the illustration reproduced above.

They had grown slowly without causing any discomfort over a number of years. When the patient was admitted to hospital hard rubbery nodules were found along the ulnar borders of both elbows, and a larger one on the left knee ; similar tumours, not visible but palpable and discovered by radiographic examination, were present on the right external malleolus. The skin over the nodules was freely movable and they were themselves partially movable. The histological appearances are described and illustrated. The authors discuss as possible aetiological factors, small repeated traumata, untreated syphilis, and the tendency of negroes to form fibrous tissue—the latter discounted, however, by the occurrence of such growths in white persons. Response to treatment seems to depend largely on the age of the lesions and the amount of fibrous tissue which has formed. In the authors' case the nodules on the ankle decreased in size during three months' anti-syphilitic treatment, and they mention that in a Polish woman, seen by one of them, with a nodule the size of a cherry close to an elbow, the tumour decreased by about one-half in the course of two years' treatment. *L. W. Harrison.*

LEPROSY.

British Empire Leprosy Relief Association (Madras Provincial Council). **Annual Report 1942–43** [Austin, T., Chairman, Executive Committee]. 10 pp. 1943. Madras : Govt. Press.

Further progress is reported in spite of the threatened invasion of India. Epidemiological studies were continued at the Silver Jubilee Clinic for the Study of Child Leprosy, Saidapet ; these have already been dealt with in this *Bulletin*. The most important point is that open case contact in 69·7 per cent. of the cases was traced to an intrafamilial or house contact. Seventy such open cases infected 141 children out of a total of 225 exposed to such close contact. Thus only 37·3 per cent. of the contacts showed no sign of the disease but some may still do so [see Cochrane and Rajagopalan, below). Work at a rural investigation centre includes a trial of voluntary night segregation of infective cases in villages ; the results of this plan are promising but not yet conclusive. Work at an urban investigation centre was dislocated by an emergency evacuation of the coastal area involved.

The Lady Willingdon Leprosy Sanatorium, Chingleput, discharged 141 lepromatous cases as recovered or quiescent, but from 15 to 25 per cent. have relapsed and been readmitted. The best results were obtained when the treatment was continued for six months after the symptoms had cleared up. Intradermal injections of hydnocarpus preparations have given better results than subcutaneous injections ; they are also more popular. The efficacy of avenyl in rendering

positive Wassermann reactions negative has proved disappointing. The Children's Leprosy Sanatorium at Ettapur admitted 37 boys and discharged 11 during the year. The teaching of leprosy workers is being continued. Altogether the year's record is a good one.

L. Rogers.

COCHRANE, R. G. & RAJAGOPALAN, G. **The Study of Family Susceptibility in relation to the Epidemiology of Leprosy.** *Leprosy in India.* 1943, July, v. 15, No. 3, 76–81.

This is a careful study under the favourable conditions afforded by the Silver Jubilee Clinic for the Study of Child Leprosy, at Saidapet, Madras. The important rôle of familial susceptibility has been stressed in North America by AYCOCK and MCKINLEY [this *Bulletin*, 1938, v. 35, 884], but WADE [*ibid.*, 1942, v. 39, 223] in an editorial article, concluded that there is not sufficient evidence to decide whether or not hereditary susceptibility to infection does exist. The importance of contact is very generally accepted as the greatest factor in the spread of leprosy. An analysis has therefore been made by the authors of the intrafamilial open contacts of 245 cases of leprosy among children registered at the clinic during the five years since it was opened.

TABLE I.

No. of cases with a history of intrafamilial open cases in family	245
No. of families	125
Total persons in these families (adults 442, children 330)	772
Average size of the family	6·1
Percentage of child cases to total children found in the family	56·4 per cent.

Thus more than half the children exposed to infection in the family have already shown signs of leprosy.

TABLE II.

18 Fathers have infected 27 out of 47 children ...	57·44 per cent.
8 Mothers have infected 12 out of 20 children ...	60·0 ,,
9 Maternal uncles, aunts have infected 13 out of 28 children	46·4 ,,
16 Paternal uncles, aunts have infected 21 out of 34 children	61·8 ,,
18 Brothers and sisters have infected 29 out of 50 children	58·0 ,,
30 Co-tenants have infected 41 out of 80 children ...	51·2 ,,

Thus the highest number of infecting sources is to be found in co-tenants and the number of children infected from this group is the largest of all. Further, the percentage of children infected by co-tenants and relatives respectively does not show such a marked difference as to suggest that the presence of familial susceptibility in the latter group has influenced to a greater degree the incidence of the disease in these

families, the type of contact remaining the same (household). In fact, the percentage of children infected by co-tenants is higher than those infected by at least one group of relations, the maternal uncles, aunts and cousins. Therefore it appears reasonable to conclude that the importance of familial susceptibility in leprosy is not so great a factor as some authorities suggest.

Further analysis showed that the percentage of children without signs of leprosy was 63·3 in those aged 0–4 years, 36 per cent. at 5–9 years and 32·8 per cent. at 10–14 years of age. More of the youngest children may yet show leprosy.

Moreover, an analysis of 391 families shows that the number of children infected in the different groups varied between 43·47 per cent. and 55·94 per cent.; among adults in the same families the infection rate varied between 18·51 per cent. and 21·73 per cent., irrespective of the nature of the contact in the groups. In the case of the children the highest rates were seen in two groups with open case contact in the family, in spite of the fact that family history is the same in both groups. These data also indicate that family susceptibility is not an important factor. *L. Rogers.*

Leprosy in India. 1943, July, v. 15, No. 3, 67–75. [52 refs.] **Diet and Susceptibility to Leprosy.** [Editorial.]

The first part of this article deals with evidence in support of the view that undernutrition and bad diet predispose to infectious diseases. It deals mainly with deficiencies of vitamins and concludes that a deficiency of vitamins A and C renders both experimental animals and human subjects more susceptible to infection in general and that supplementary supply of them corrects the deficiency and removes the increased susceptibility. On the other hand, there is no evidence that vitamins B and D play any important part in this respect. The addition of milk to a diet may also increase resistance to infection. The effect of diet on the more chronic disease tuberculosis is next considered and evidence is quoted in support of the view that deficiencies of vitamins C and D predispose to tuberculous disease in white rats and guineapigs. The increase in human tuberculosis after the war of 1914–18 is also considered to have been influenced by deficient diet, and some experimental evidence is quoted in support of this view.

Leprosy is then considered. The evidence of Tonkin that animal protein is absent from the diet of highly leprous tribes of Nigeria, and of Atkey [this *Bulletin*, 1934, v. 31, 542; 1935, v. 32, 348] that the disease is rare in milk-consuming Arabs in the Anglo-Egyptian Sudan, is quoted. The high incidence of leprosy in the rice-eating peoples of Bengal and other parts of India and in China is also referred to. Maxwell reported an increase of leprosy in the province of Hupeh in Central China after flood and famine. The foregoing evidence is not conclusive in the absence of confirmatory experimental work because it has not been proved that the diet was more deficient than that of families without leprosy cases. With regard to vitamins, Japanese workers have found deficient excretion of vitamins B_1 and C in the urine in leprosy, and in lepromatous cases the C content of the aqueous humour of the eye was much decreased. Uchida found that in rats infected with experimental leprosy vitamin A, but not B_1, prevented the occurrence of morbid changes. However, Badger *et al.* [this *Bulletin*, 1941, v. 38, 29] have reported a shorter incubation period of

inoculated rat leprosy when B_1 was deficient. GAVRILOV *et al.* have reported similar results in guineapigs, but other observers report variable results with the different vitamins.

The general conclusion is that states of malnutrition and undernourishment do predispose to infection with leprosy, but further experimental work, together with field studies, is required to clear up the matter. *L. Rogers.*

SOLSONA CONILLERA, J. Estudio sobre la endemia leprosa en nuestro Protectorado Marroqui. **Leprosy in the Morocco Protectorate.** *Med. Colonial.* Madrid. 1943, Jan. 1, v. 1, No. 1, 29–52, 12 figs. & 2 maps. [39 refs.]

It was in 1929 that Luengo GARCIA recorded the first cases of leprosy to be seen in Morocco and in 1943 Dr. MONTAÑÉS of the Fontilles Leprosarium noted only four cases in Ceuta. The author states that there were 56 names on the register, seven imported and 49 indigenous. Twenty-five were in Gomara, 14 in Lucus, nine in Tetuán, five in Tangier, and three isolated cases. As for nationality, four were Spanish, 41 Moroccans in the Spanish zone, nine in the French zone, one Portuguese, and one unknown. Forty-six were males: only 10 were females. None was under the age of 10 years, and in succeeding decades the numbers were 5, 8, 14, 15, 5: four were between 60 and 80; the ages of five were not known. Twelve were suffering from the cutaneous form, 40 from the mixed, none was recorded of the purely nervous type, but of four the clinical form was not stated. Photographs of patients have been well reproduced. Nothing is said as regards medicinal treatment. Prophylaxis is on the usual lines. *H. Harold Scott.*

PARK, F. R., KITCHELL, J. R. & SHEPHERD, S. G. **A Case Report of Cutaneous Leprosy with a Brief Discussion of the Classification, Treatment, and Epidemiological Portent.** *Ann. Intern. Med.* 1943, Nov., v. 19, No. 5, 805–8.

This is a case of sporadic leprosy in which the failure of early diagnosis exposed the community to some danger of infection. The patient was a Russian Jew admitted to a Philadelphia hospital for fractured femur and later treated in a nose and throat clinic for chronic hypertrophic rhinitis. Two and a half years later, after unsuccessful treatment for atypical Buerger's disease, a leonine facial appearance and facial nodules led to microscopical examination which revealed abundant bacilli like *Myco. leprae.* It was then learned that the patient's wife had died of leprosy eight years previously and he had moved to another city to avoid surveillance by the local Department of Public Health. He had been seen by many physicians, who overlooked the disease although the leonine appearance had been noted on his first admission to the Philadelphia hospital. He is now considered to be a mixed case with both lepromatous and neural symptoms. This case should be borne in mind in view of the return after the war of soldiers infected with leprosy while on service in endemic areas of leprosy, such as occurred in Great Britain and the U.S.A. after the Great War of 1914–18. *L. Rogers.*

Fiol, H. & Blanco, J. F. Lupus eritematoso generalizado y atipico en un enfermo de lepra. [**Atypical and Widespread Lupus Erythematosus in a Leper.**] *Rev. Argentina Dermatosifilologia.* 1943, Dec., v. 27, No. 4, 559–67, 5 figs.

An Argentine, 28 years of age, showed signs of anaesthetic leprosy in 1930; later, maculae and nodules appeared. He had treatment, but irregular and inadequate, and in 1939 was classified as L_2. With chaulmoogra ethyl-esters his state improved, but the following year he developed erythematous and achromic patches, squamous in parts, involving the nose and cheeks (butterfly patch), the scalp, submaxillary and mastoid regions, the forehead, neck, throat and arms. This was at first diagnosed as psoriasis, but on further consideration and as the result of biopsy examinations the diagnosis was changed to lupus erythematosus. The Mantoux reaction was positive, Mitsuda negative, Kahn presumptive positive, Wassermann and Kahn standard doubtful. Treatment was by chaulmoogra and bismuth alternately. It was particularly noted that as the lupus erythematosus developed the lepromata which had been progressing began to recede. The author suggests the possibility of a relative immunity between a developing lupus erythematosus and an established leprosy. *H. Harold Scott.*

Dubois, A. Formes de passage de la lèpre neurale à la lèpre lépromateuse. [**Transition of Neural into Lepromatous Leprosy.**] *Ann. Soc. Belge de Méd. Trop.* 1943, Mar. 31, v. 23, No. 1, 13–17.

Three cases met with in the Congo area are recorded which illustrate an unusual sequence of events, the occurrence of which has been much discussed recently by Rodriguez, Wade and Plantilla [this *Bulletin*, 1940, v. 37, 630] and others. The first showed numerous simple neural macules and mutilations, together with numerous lepra bacilli in the skin of the ears. The other two presented minor tuberculoid neural macules together with positive thickened ear lesions in one and positive infiltrated lesions on an arm and on the back in the other. Two other cases are quoted from other writers. The author thinks his cases could legitimately be classed as mixed leprosy infections. *L. Rogers.*

Faget, G. H., Pogge, R. C., Johansen, F. A., Dinan, J. F., Prejean, B. M. & Eccles, C. G. **The Promin Treatment of Leprosy. A Progress Report.** *Pub. Health Rep.* Wash. 1943, Nov. 26, v. 58, No. 48, 1729–41, 8 figs. on 2 pls.

Promin (Parke Davis & Co.) is the sodium salt of p.p. diaminodiphenylsulphone n.n. didextrose sulphonate. It has been used with success in experimental tuberculosis of guineapigs. Two years' use shows it to be the best of the sulphonamides for the treatment of leprosy. No specific action of the drug on Hansen's bacillus is known. It is too toxic for use orally. Intravenously 1 to 5 gm. daily on six days of the week were given, mostly 5 gm. doses continued with one or two weeks' rest, three times a year, up to two years.

Toxic manifestations.—Anaemia occurs in 46 per cent. after eight weeks' intravenous treatment. Blood counts were done every two weeks. A fall to 3·5 million erythrocytes took place in 71 per cent. and to 3 million in 9 per cent. If there is a fall to under 4 million ferrous sulphate or ferrous carbonate should be given, and if a further

fall occurs oral liver preparation should be given; promin treatment should be discontinued while the count is below 3 million and liver extract should be given parenterally, with iron by the mouth. Promin can be resumed when over 3·5 million. Leucopenia occurred in only 3 per cent.; injections should be stopped if leucocytes fall below 3,000. Allergic dermatitis necessitates stopping injections, which can be resumed with 0·1 gm., gradually increased to 2 gm. doses, when the dermatitis has disappeared. It occurred in 16 per cent. Two-thirds have been desensitized. Nausea occurred in 35 per cent., vomiting in 7 per cent.; they were transitory and preventable by taking one minute to inject 5 gm. promin. Acute lepra reactions are less frequent than with other treatments. Exacerbation of old irido-cyclitis occurred in 10 per cent., but was of a temporary nature except in one case. Lymphadenitis was rare and subsided on reducing the dose to 1 gm.

Clinical material.—All were positive bacteriologically and nearly all lepromatous cases not doing well were included, so it was a severe test. Patients with eye, nose and throat complications as a rule showed a marked improvement. Epistaxis occurred. Six cases with advanced lepromatous laryngitis improved, as did lesions of the lips, tongue, gums and palate. Twenty-two case reports are given and photographs before and after one or two years' treatment show marked improvement in lepromatous cases. Table I shows the results in 21 mixed or advanced lepromatous and one neural case. Improved 15, stationary 6, worse 1; all the patients were treated for one year or over; five of them became negative for bacteria. Table II shows 46 cases in which a shorter course of treatment was given; all but six were lepromatous: Improved 26, stationary 17, worse 3, became bacteriologically negative 7.

In other cases a drug, Internal Antiseptic 307 (Parke Davis) sodium 4,4′-diaminodiphenylsulphone-2-acetylsulphonamide), closely allied to promin, has been given orally in doses of 5–15 grains daily, average dose 10 grains daily, with controls taking a placebo. After eight months the disease was seen to be checked in a number of cases. In all cases the urine was examined every two weeks but no kidney damage was noted.

It is claimed that although "as yet no case of leprosy has become arrested," the progress of leprosy was inhibited in a number of cases, and promin is the sulphonamide drug which thus far "seems to possess to the greatest extent some chemotherapeutic properties against leprosy." *L. Rogers.*

DE CAIRES, P. F. **Iron Therapy in Severe Cutaneous Leprosy.** *British Guiana Med. Ann.* 1943, 132–6, 1 chart.

The author has been making routine estimations of the haemoglobin in the blood of patients with leprosy at the Mahaica Leprosy Hospital, British Guiana. In lepromatous cases in an advanced stage it averaged only 50·75 per cent., against 85·24 per cent. in a control group of healthy non-leper attendants. In able-bodied patients of all types it averaged 62·85 per cent., in children with active symptoms, 62·55 per cent., and in recovered cases it was from 68·69 per cent. to 72·55 per cent. Cases with septic complications were excluded from the estimations and hookworm infestation was also absent. These observations led to the administration of Ferri et Ammon. Citras in 30 gr. doses three

times a day with beneficial results, in addition to the routine anti-leprosy treatment by injections of hydnocarpus esters. *L. Rogers.*

HELMINTHIASIS.

EIGENFELD, D. D. & SCHLESINGER, C. J. **An Improved Flotation Method for the Recovery of Ova from Feces.** *J. Amer. Vet. Med. Ass.* 1944, Jan., v. 104, No. 802, 26, 1 fig.

This is a simple contrivance to enable the surface layer, containing the ova, to be collected easily and completely. The floatation tube has a side outlet in its upper part through which the surface layer overflows

Illustrating the use of a side-arm tube for collecting the surface film from a faecal suspension.

[Reproduced from the *Journal of the American Veterinary Medical Association.*]

when it is raised by the addition of more floatation fluid through a funnel as shown in the diagram. Distilled water is added to the centrifuge tube which is then centrifuged and the deposit examined for ova.

J. F. Corson.

PITTA SIMÕES, J. M. & HILL, R. B. Resultado dum inquérito sobre a infestação, por helmintas, das creanças de Aguas de Moura. [**Helminth Infestation of Children in Aguas de Moura.**] *An. Inst. Med. Trop.* Lisbon. 1943, Dec., v. 1, No. 1, 97–104. [11 refs.] English summary.

"A survey on the infestation of children up to 15 years of age was carried out in Aguas de Moura. All children in the locality were

examined and it was found that out of 115 children observed, 16 were infested.

" As in 4 children more than one species of parasites was found, the number of cases comes up to 21.

" According to the species of the parasites, the distribution of the cases is as follows :—

H. nana	10 cases
T. trichiura	8 ,,
E. vermicularis	2 ,,
A. lumbricoides	1 ,,

MILLER, J. J., Jr. & WILBUR, D. L. **Paragonimiasis (Endemic Hemoptysis). Report of 3 Cases.** *U. S. Nav. Med. Bull.* 1944, Jan., v. 42, No. 1, 108–17, 2 figs.

The authors have diagnosed, by finding the operculated eggs in fresh, unstained sputum, three cases of infestation with *Paragonimus westermanni* among members of the United States Naval and Marine Corps returning from the South Pacific (Samoa, Solomon Islands). Since this paper was written, they have diagnosed in the same way four other cases from Samoa which showed characteristic pulmonary symptoms.

After discussing the life history of the parasite, and the pathology and symptoms of paragonimiasis, the authors describe the three cases just referred to. The striking clinical features were similar in all three, namely, persistent chronic cough, pain in the chest and expectoration of several ounces of very sticky, colourless sputum containing small brown flecks. Only one of the three subjects, an officer aged 23, showed haemoptysis. Before he left the United States, he had had a fall from a horse and then coughed up blood on one occasion. Four months after his arrival in Samoa, where he underwent a period of intensive training in the jungle and underbrush, he began to complain of cough, weakness, and pain in the left leg and lower half of the chest. He coughed up brownish material and later blood, until he fainted after a haemoptysis of about 500 cc. Subsequently, while he was on a transport, he coughed up occasionally as much as 200 cc. of blood. Under treatment with emetine he was, at the time of writing, slowly recovering.

This patient showed a type of pain in the chest which is unusual in the authors' experience of such cases ; it was deep in the chest, difficult to localize, constant, made worse by severe cough but not by breathing, and was partially eased by immobilization of the chest by strapping. X-ray examination revealed a lesion at the base of the right lung, simulating bronchiectasis. Another striking feature of this case was a persistent thrombo-phlebitis of one leg, with constant pain in the tibial region, accompanied by hyperaesthesia over the same region. Another of the patients had pain in the left knee, thigh and inguinal region, attributable to thrombo-phlebitis with some oedema ; he also had enlargement of the superficial abdominal veins, suggesting obstruction of the inferior vena cava and possibly of the portal vein.

The disease is rare in the United States, and all of the few cases known have been in persons who have lived for some time in the Orient. Human or other mammalian infection results from eating raw or improperly cooked crab or crayfish.

[Paragonimiasis is found in New Guinea, the Dutch East Indies India, China, Indo-China, Thailand, Malaya, the Philippines and in Korea, Japan and Formosa. Cases have also been reported from West Africa.] *G. Lapage.*

KEVORKOV, N. P. [**Some Critical Remarks about the Epidemiology and Epizoology of *Hymenolepis* Infection.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1943, v. 12, No. 2, 80–83. [In Russian.]

The author summarizes briefly some of the world literature on the question whether *Hymenolepis nana* of man and *H. murina* of mice and rats are the same species. Much work has been done on this question in the U.S.S.R. With SCHLEICHER the author examined in Tashkent 125 rats (*Rattus turkestanicus*, the only species of rat found in Uzbekistan). Of these seven (5·6 per cent.) had *H. murina*. During the same period of years it was found that 1·6 per cent. of 188 mice (*Mus musculus*, house mouse) examined had *H. murina*. A table summarizing the percentages of rats and mice harbouring *H. murina*, according to the results of workers in various parts of Russia (*e.g.* Moscow, Don Basin, Odessa, Kharkov, Tashkent), shows that rats are much more heavily infested than mice. The work of the author and of other Russian workers indicates that there is little coincident infestation of man and rodents with *Hymenolepis* in various parts of Russia, although this does occur in some regions. CHANDLER gives two reasons for this lack of correspondence between the incidence in man and rodents. First, he thinks that man gets the infestation with greater difficulty in civilized towns than in places where hygiene is primitive (*e.g.* India), and second, that the eggs of *Hymenolepis* are sensitive to cold and quickly perish in moderate climates, whereas rats easily infest each other by coprophagy. Discussing his own and other criticisms of these views, the author records his experiments in collaboration with REPKIN, which showed that the eggs of *Hymenolepis* dried up, under the conditions prevailing in Tashkent, in 5–15 minutes; their conclusion was that higher temperatures are more harmful than lower ones to the eggs. The author concludes, however, that man can become infested with *Hymenolepis* from the rat, which can act as a reservoir of the infestation. *G. Lapage.*

KEVORKOV, N. P. [**On some Problems of the Treatment of *Hymenolepis* Infection.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1943, v. 12, No. 2, 83–8. [In Russian.]

Remarking that tens, or even hundreds, of thousands of specimens of *Hymenolepis nana* may occur in a human patient, especially in children, the author says that one treatment may be sufficient only in exceptional cases and that 3–5 treatments (with *Filix mas*) may not expel all the parasites. This unsuccessful treatment is due, he thinks, first to the position of the parasites in the lower third of the small intestine, and to the mechanism of the movement of the contents of this part of the intestine. In 1930 he himself swallowed eight gelatin capsules filled with barium and found, by means of X-ray photographs, that the capsules opened in the stomach, but that the barium travels very slowly down the small intestine. When dogs were given bread and magnesium sulphate to evacuate the intestine and then male fern extract, it was found at post mortem that, in one dog given 2·0 [? gm.]

the male fern travelled 180 cm. from the pylorus in 3½ hours, in another, given 1·0, 160 cm., in 2 hours 10 minutes, in a third given 1·0, 120 cm. in 3½ hours, and in a fourth given 8·0, 132 cm. in 2 hours 10 minutes. He calculates that children aged 5–7 years have a small intestine 483 cm. long ; they are given a dose of 1·0 of male fern ; at the age of 13–14 it is about 500 cm. and they are given 2·0 of male fern. In both cases the male fern will not get, in the course of 3½ hours, to the end of the small intestine. A further 3 metres of intestine remain which cannot be reached by the extract in time. Even if there were time, less and less of the extract is available as it progresses down the intestine. Its slow progress depends, not on the quantity given, but on the peristalsis and on the tendency of the extract to adhere to the walls of the intestine.

Experiments show, moreover, that we cannot kill all the parasites when their numbers are so great, because, for the reasons given, only relatively small amounts of the extract get to the lower parts of the intestine where most of the parasites are. Clinical study of cases shows that there may be no symptoms at all and the question then arises whether the male fern may not cause greater damage (to the heart muscle) than the parasites are causing. When, however, there are symptoms, subjective or objective, we should treat the cases. The author has found that the fractional-dose method of PODIAPOLSKAYA for giving male fern produces the quickest effect in comparatively small doses. [No details of this method are given.] As regards prophylaxis, it is doubtful whether we know enough about the epidemiology of the infestation to carry this out satisfactorily.

G. Lapage.

IONINA, N. C. [**The Clinical Study and Treatment of** *Hymenolepis* **Infection.**] *Med. Parasit. & Parasitic Dis.* Moscow, 1943, v. 12, No. 2, 95–6. [In Russian.]

After treating 37 cases of infestation with *Hymenolepis nana* (4 were adults, 3 children aged 14–15, 22 children aged 10–13 and 8 children aged 5–9), the author concludes that the efficiency of the treatment with male fern by standard methods is not great (24·1 per cent. in his experience). The efficiency of treatment with pumpkin seeds is still less (14·2 per cent. in his experience). A new method of treatment is required. The author worked in the Tadzhik province (Uzbekistan). *G. Lapage.*

HEILIG, R. & VISVESWAR, S. K. **Does a Hookworm Toxin exist ?** *Indian Med. Gaz.* 1943, Dec., v. 78, No. 12, 578–83. [18 refs.]

Discussing the causation of hookworm anaemia, the authors agree that loss of blood is certainly one factor, but point out that the severest anaemia may occur when there is apparently only a minute loss of blood. Malaria, malnutrition, faulty food habits and multiple infections might depress the haemopoietic activity of the host so much that even small amounts of blood could not be replaced, especially when protein and iron are not supplied or utilized in sufficient amounts. It has been suggested that a toxin produced by the hookworms also operates, which either paralyses the bone marrow or causes haemolysis or does both. But it has been definitely shown that there is no increased blood destruction. The idea that there may be an aplastic

anaemia due to the action of a hookworm toxin on the bone marrow is unlikely, because, if it is true that iron, arsenic, etc., cannot exert any effect on an aplastic anaemia, hookworm anaemia cannot be of this type ; no anaemia responds so promptly to iron treatment.

Heilig [this *Bulletin*, 1943, v. 40, p. 68] has, however, found that in 6 out of 65 cases of hookworm anaemia there was no improvement of the heart condition under iron treatment until deworming was complete, although there was considerable increase of haemoglobin and of the numbers of erythrocytes. When, however, deworming is complete in such cases, the heart condition improves quickly, even when the haemoglobin values and the number of the erythrocytes remain constant. He concluded that the anaemia and the heart condition are caused by different factors, that the anaemia is not necessarily the cause of the heart condition and that something directly connected with the presence of hookworms prevents the heart improvement, even when abundant iron reduces the effect of the parasites on the blood.

To test this idea the authors took 26 patients with severe hookworm anaemia and no other active disease. Massive doses of iron (90 grains of iron daily in the form of Blaud's pills) were given. When the haemoglobin reached 35–40 per cent. (Sahli), deworming was done with carbon tetrachloride and oil of chenopodium. The iron was stopped from the day before deworming until the end of the experiment, so that any changes observed could be regarded as not being due to the iron medication. Haemoglobin estimations and enumerations of erythrocytes were made every week ; electrocardiograms were taken three times before treatment, on the day before deworming and one week after deworming. At the same times blood serum was taken and used for perfusing isolated frog's hearts. This was done by independent workers using Gunn's modification of Trendelenburg's method. It could only be done with the sera of 14 of the 26 patients. The results are tabulated and discussed. A well-marked reduction of the amplitude of the beat of the frog's heart, sometimes visible by direct observation, was recorded, but the paper should be consulted for details of this aspect of the experiment.

The authors claim that it is possible to distinguish between the effect of hookworm anaemia and the effect of another factor toxic to the heart muscle. There is no doubt, they think, that iron treatment and blood regeneration cause a very considerable improvement in the myocardium and reduce or abolish, in a high percentage of cases, the depressant effect of the serum of hookworm patients on the frog's heart. But in a minority of cases, although improvement occurs after deworming, it does not occur after anti-anaemic treatment, a fact which suggests the presence in the blood of a myocardiotropic factor connected with the presence of the hookworm. When improvement occurs in spite of the action of this factor, it is due to overcompensation of its effects by blood regeneration.

The least probable explanation of this factor is to call it a chemical toxin produced by the worms ; it is more probable that it is a toxin in the serological sense and we are reminded that antibodies have been found in the blood of dogs infested with *Ancylostoma caninum*. If this view is correct, iron therapy or increased haemopoiesis would stimulate antitoxin production, so that all toxins would be neutralized in a majority of cases. In a minority, perhaps because of " weakness of the reticulo-endothelial system," some un-neutralized toxin would

remain, so long as some worms remained; and this would prevent recovery of the myocardium and maintain the depressant effect of the serum demonstrated by the perfusion of the frog's heart, although it could not suppress the blood improvement.

The existence of an anti-haemopoietic toxin has not been proved and is improbable. *G. Lapage.*

Caetano da Silva Júnior, J. A. & Flosi, A. Z. Sobre um caso de meningopatia secundária a ascaridiose. [**A Case of Meningitis Secondary to *Ascaris* Infection.**] *Rev. Neurol. e Psiquiatria de São Paulo.* 1942, Sept.–Oct., v. 8, No. 5, 183–6.

Claveaux, E., Salveraglio, F. J., Magnoni, P. & Canzani, R. Estudio clinico epidemiologico de un foco de triquinosis. [**A Clinical and Epidemiological Study of an Outbreak of Trichiniasis.**] *Primer Congr. Nac. Enfermedades Endemo-Epidémicas, Buenos Aires, 1942, Nov. 9–13.* 517–37.

The authors describe in detail an outbreak of trichiniasis at Pueblo Soca, 60 kilometres from Montevideo. Brief histories of 69 cases are given and the symptoms and differential diagnosis are discussed. None of the patients died. All the symptoms and signs discussed have been reported in this *Bulletin* in recent abstracts of papers on outbreaks in Germany and elsewhere. Among the gastro-intestinal symptoms special attention is directed to the " boiled " tongue (from its resemblance to boiled meat) seen during the febrile stage, to the anorexia and attacks of gastro-intestinal atony with flatulent crises. No serious cardio-vascular or urinary symptoms were seen and the nervous system was affected in only two cases. One of these slowly developed, 96 days after the onset of the illness, progressive unilateral paralysis of the face which began with disturbance of taste and transitory diplopia; after 45 days it had disappeared. The other had for 15 days marked loss of strength in his arms with decreased tendon reflexes and some zones of anaesthesia; these also disappeared completely. Transitory acute pulmonary symptoms with eosinophilia suggesting Löffler's syndrome were very common and should suggest search for Trichinella. Cases with pulmonary signs are divided into (1) those with areas of transitory consolidation of the lung with rise of temperature, cough and expectoration of muco-purulent or sanguineous sputum free from acid-fast bacilli; and (2) those with pleuritic signs, especially at the base of the thorax. These explain the thoracic pain of some cases and may correspond to localization of the infestation at the insertions of the diaphragm. The blood showed extraordinarily high eosinophilia, which rose, in some cases, to 50 or 60 per cent. and, in one case, to 72 per cent., with 20,000 leucocytes per cmm. This eosinophilia, like the clinical signs, persisted for weeks or months. The number of leucocytes varied; in patients with marked clinical symptoms there was usually a leucocytosis of 15,000–25,000 per cmm.; two showed a moderate leucopenia and in others there was a normal number of leucocytes. In some cases transitory positive serological reactions suggested syphilis and two cases had been so diagnosed. Patients whose blood serum gives positive results in Wassermann or Kahn tests and who have no history of syphilitic infection, should be examined for Trichinella. In some cases the allergic signs, urticaria, transitory oedemas, joint pains, eosinophilia, etc., may be the only signs and in many cases symptoms

are so slight that they escape diagnosis. Probably there were many of these in the local population which were not seen. The infestation was found in the families of most of the patients seen and also in the children of a local public school. The epidemic began at a time when pork from uninspected sources was being largely consumed in Pueblo Soca, but the source of the infestation was not found, nor was Trichinella found in the local rats examined. All examinations of the blood, faeces and excised muscle were negative. No precipitin tests were done, but the intradermal test of Bachman, done on seven cases, was positive in all and negative in 33 controls except three, one of which had a heavy infestation with Trichuris (group reaction), the other two having symptoms suggestive of trichiniasis. Brief reference is made to other cases noted in Argentina, Santa Fé and Uruguay. In five cases subcutaneous nodules, smaller than a grain of maize, occurred all at about the same time (at the end of the illness) and all at the level of the insertion of the external border of the rectus abdominis into the costal margin. From this they apparently migrated for about 5 cm. in various directions, their track being marked by a fibrous cord slightly tender to pressure. *G. Lapage.*

WRIGHT, W. H., KERR, K. B. & JACOBS, L. **Studies on Trichinosis. XV. Summary of the Findings of *Trichinella spiralis* in a Random Sampling and other Samplings of the Population of the United States.** *Pub. Health Rep.* Wash. 1943, Aug. 27, v. 58, No. 35, 1293–313. [22 refs.]

This paper is reviewed in *Bulletin of Hygiene*, 1943, v. 19, 201.

DEFICIENCY DISEASES.

LUCKHOFF, C. A. **Evidence of Vitamin B Deficiency in Orange Free State Natives.** *South African Med. J.* 1943, Dec. 25, v. 17, No. 24, 375–6, 4 charts.

Of 4,600 natives of the Orange Free State examined clinically, recognizable vitamin B deficiency was found in 1·9 per cent. These figures take no account of subclinical deficiency. The condition was not common in children or pregnant women, and males were affected more frequently than females in the proportion of 5 : 2. The only aetiological factor appears to be a deficient diet. These natives live chiefly on maize, and the majority of the affected persons (75 of 86) used a refined maize meal from which the husk, and a portion of the germ, had been removed. Animal products, vegetables and fruits are rarely taken. Nevertheless, the great bulk of the population subsists on this diet, supplemented by native beer, yet only a proportion show signs of deficiency. In general the people appear to be fit and active, and by no means thin. The energy value of the normal diet is about 2,000 calories, with a carbohydrate-protein-fat ratio of 16 : 2 : 1. It seems probable that some other factor is necessary to precipitate overt deficiency disease, and the author speculates on the effect of intercurrent disease (alcoholism, diarrhoea, sprue and cirrhosis of the liver) and other factors. [The reference to sprue is interesting, but no details are given. MANSON-BAHR (The *Dysenteric Disorders*, 2nd

Edition, 1943) notes that few authentic cases have been reported from Africa, but quotes one from Nyasaland.] He points out that the use of beer did not prevent avitaminosis in 36 patients accustomed to take it.

Pellagra (30 cases) is frequently seen, beriberi (4) rarely. In addition there is a condition resembling tabes dorsalis, and another in which various skin manifestations occur alone or associated with pellagra or beriberi. A characteristic anaemia is also found; this and the neurological condition are to be described later. In pellagra the gastro-intestinal symptoms are not prominent, but anorexia is common; mental changes are much in evidence and symmetrical skin lesions frequently seen. Skin lesions other than those associated with pellagra are described :— areas of pigmentation and desquamation on the anterior aspect of the forearm, the abdomen, cheeks and forehead; keratosis and pigmentation of the dorsum of the forearm just below the elbow. Eczematous patches at the angles of the mouth, with conjunctival hyperaemia, are regarded as signs of riboflavin deficiency. These skin conditions are successfully treated by Marmite or other substances rich in vitamins of the B group. *Charles Wilcocks.*

i. Watson, C. J. & Layne, J. A. **Studies of Urinary Pigments in Pellagra and other Pathological States. I. Clinical Observations.** *Ann. Intern. Med.* 1943, Aug., v. 19, No. 2, 183–99. [44 refs.]

ii. Layne, J. A. & Watson, C. J. **Studies of Urinary Pigments in Pellagra and other Pathological States. II. The Excretion of Porphyrin and the Urorosein Reaction in Dogs with Experimental Blacktongue.** *Ibid.* 200–205.

iii. Schwartz, S., Marvin, J. F., Layne, J. A. & Watson, C. J. **Studies of Urinary Pigments in Pellagra and other Pathological States. III. Certain Toluene Soluble Pigments of Human and Canine Urine.** *Ibid.*, 206–12, 5 figs.

In a previous communication Watson pointed out that the Ellinger-Dojmi colour reaction is due to urorosein and that porphyrin, although capable of yielding colour if present in sufficient amounts, was not the source of the positive reactions encountered in urine samples from a variety of conditions, including pellagra. Beckh, Ellinger and Spies had employed this reaction for the quantitative estimation of porphyrin in the urine. They stated moreover that the administration of nicotinic acid was followed by a prompt fall in the excretion of urinary porphyrin to normal levels. This led to a considerable literature, all based on false premises.

In the present three communications the urinary pigments in pellagra, etc., are put on a proper basis. The authors' conclusions are as follows :—

i. "1. The chromogen of the urorosein reaction is a normal constituent of the urine of many individuals who have no clinical evidence of nicotinic acid deficiency. The available evidence indicates that this chromogen is indol-acetic acid.

"2. The development of the urorosein reaction either by the method of Nencki and Sieber, or that of Beckh, Ellinger and Spies, requires the presence of nitrite or a similar oxidizing agent. Substances of this type are native to urines which exhibit spontaneous reactions. The exact nature of these native substances remains to be determined.

" 3. No definite correlation has been noted between the presence and disappearance of either chromogen or oxidizing agent, with the deficiency or administration respectively, of nicotinic acid. The results of the present investigation indicate, however, that spontaneous reactions (without addition of nitrite) occur only in association with disease and much more frequently in subjects having deficiency states.

" 4. The Ellinger-Dojmi color reaction, on which the B.E.S. test is based, is not at all specific for porphyrin, and in our experience has always been due to urorosein.

" 5. The development of a red color in the toluene preservatives of pellagra urines, also of urines from certain patients with malnutrition of one cause or another, could not be correlated with other evidence of nicotinic acid deficiency. This pigment has not been observed to develop in urines of normal individuals."

ii. " 1. The spontaneous urorosein reaction was consistently negative in urine samples from dogs having experimental blacktongue.

" 2. The appearance of red color in the toluene preservatives of dog urines was not correlated in any way with nicotinic acid deficiency.

" 3. There was no significant increase in coproporphyrin excretion in dogs with blacktongue over that observed during the control periods."

iii. " 1. The red pigment extracted by toluene from certain human and canine urines (papers II and III) has been shown by means of chromatographic analysis to be composed of several similar pigments.

" 2. Two pigments each from human and canine urines were found very similar to, but not identical with, synthetic indirubin. On the basis of chromatographic analysis and spectral distribution curves, the latter was likewise shown to be a mixture of related pigments, none of which was entirely identical with any of those from the urine."

H. S. Stannus.

HAEMATOLOGY.

FAWDRY, A. L. **Erythroblastic Anaemia of Childhood (Cooley's Anaemia) in Cyprus.** *Lancet.* 1944, Feb. 5, 171–6, 2 figs. [21 refs.]

The characteristics of the disease described by COOLEY were a chronic and ultimately fatal anaemia of early onset in children o Mediterranean stock, with splenomegaly, peculiar bone changes, most conspicuous in the skull, a familial incidence, the presence of large numbers of nucleated erythrocytes in the peripheral blood, and a mongoloid facies which is due partly to changes in the bones of the face and partly to the pallor of the skin. Since the time of the original description similar syndromes have been found, in which one or more of the above features may be absent.

An analysis of 20 cases seen in Cyprus in 2½ years showed a preponderance of the disease in males, a febrile onset, a history of earth eating, no mental retardation despite gross physical changes, mongoloid features constant but of varying degree, cardiac enlargement, radiologically demonstrable bone changes with thickening and distinctive radial striation of the calvarium, although this was not constant. The subjective severity of the disease was entirely a function of the degree of the anaemia, which was remarkably constant over long periods. It appeared to lack correlation with the age of the patient, date of onset of the disease, bone changes or numbers of nucleated erythrocytes. The anaemia was always hypochromic, and of the nucleated erythrocytes in the peripheral blood the vast majority were normoblasts, although in most cases there was a small proportion of more primitive cells; target cells [erythrocytes with lightly stained zone between deeply stained centre and periphery] were present in 50 per cent. of patients. Bone marrow films showed an enormous preponderance of normoblasts, and the cells of the red cell series were about six times as numerous as all the white cells.

No evidence was obtained that the disease was due to malaria or leishmaniasis, or that it was secondary to rickets, tuberculosis, gastro-intestinal disturbance or syphilis. Although the red cell fragility was not examined, the absence of icterus, the low colour index and the degree of poikilocytosis served to differentiate the disease from familial haemolytic icterus. The large numbers of circulating nucleated erythrocytes, the enlargement of liver, spleen and lymph glands, the bone changes and the excessively erythroblastic marrow distinguish it from iron-deficiency anaemia; furthermore, none of the cases showed the slightest improvement when iron was given by mouth. Blood transfusions and liver extract also produced only inconstant and transitory improvement. There was no evidence of any association with pernicious anaemia or of any defective absorption of a haemopoietic factor. Although there is obviously a need for a precise study of the Rh-antigen in families affected with Cooley's anaemia, the interval between birth and the onset of the illness makes it unlikely that there is much in common between the disease and erythroblastosis foetalis.

The cause of Cooley's anaemia is quite obscure. Some intrinsic defect of the haemopoietic tissues has been favoured by most as the likely aetiological factor, but the responsibility of an infective organism, or the deficient absorption or utilization of some haemopoietic substance, cannot be ruled out. If the blood changes are inexplicable in the present state of knowledge, the bone changes are even more so. Among the suggested factors involved in the latter are the mechanical disturbance of the bone architecture by the hyperplastic marrow, the development of bone over a long period in surroundings where the supply of minerals and vitamins is probably adequate but that of oxygen deficient, and the close physico-chemical interrelationship of ionic calcium and ionic iron, in view of their competition for phosphate in the intestinal tract. *F. Murgatroyd.*

EVANS, R. W. **The Sickling Phenomenon in the Blood of West African Natives.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1944, Feb., v. 37, No. 4, 281–6, 1 fig. [10 refs.]

The incidence of the sickle cell trait was investigated in approximately 600 West African natives. Various techniques were used;

in some cases capillary blood was examined after standing at room temperatures for up to 36 hours in vaselined-sealed cover glass preparations, while in others venous or finger blood was withdrawn into citrate solution, placed immediately under liquid paraffin, and after standing for 24 hours the cells were fixed by the addition of 10 per cent. formaldehyde in saline. No significant differences were observed in the results obtained by the two methods. Blood obtained by sternal puncture was also examined. Tests for sickling *in vivo* were also made by drawing blood into paraffined syringes and placing immediately in 10 per cent. formol saline under liquid paraffin.

When sickling, the cells first expand, then assume a spheroidal shape, after which they become transformed into the multi-pointed sickle forms. In capillary preparations the reticulocytes took longer to sickle than did the more mature erythrocytes.

In some instances the cover glass examinations were made on slides on which previously a 1 per cent. solution of brilliant cresyl blue in 90 per cent. alcohol had been spread and allowed to dry. It was confirmed that the dye inhibited the formation of sickle cells ; one case in which, normally, 90 per cent. of the cells sickled in 15 minutes, showed in the presence of the dye no sickling after 6 hours and only 15 per cent. of the cells were sickled in 12 hours.

Of 224 West African native soldiers from Nigeria, 22·3 per cent. had erythrocytes which sickled *in vitro* ; of 138 from the Cameroons the percentage was 15·2 ; of 132 from the Gold Coast it was 16·6 ; and of 67 from the Gambia the figure was 28·3 per cent. It may be assumed therefrom that the incidence of the trait in British West African male natives is about 20 per cent., which figure is roughly three times as high as that found for American coloured patients by various workers. Six cases of sickle-cell anaemia, of which four were fatal, were included among Gambian natives. The high figure for Gambian soldiers may be due to the relatively small number examined and to the high degree of in-breeding. Excluding patients considered to be suffering from sickle-cell anaemia, the mean red cell count of the soldiers whose blood showed the sickle-cell trait was 4,100,000 erythrocytes per cmm. and that of those not showing the trait 4,250,000.

In a small group of 46 males and 23 females, mostly members of one large " family " (*Bojang*) in a Gambian village, the total incidence of the sickling trait was 18·8 per cent., with an incidence of 22 per cent. among the males and only 13 per cent. among the females. In this group one family representing the parental, first and second filial generations respectively, and comprising 12 males and 10 females, gave figures of 5 for the males and 1 for the females. Thus of the remaining 47 members of the group (34 males and 13 females) only 15 per cent. had cells which sickled, which is of interest, as the trait is inherited as a Mendelian dominant character.

Subdividing the soldiers it was found that among 259 suffering from chronic disease the incidence of sickling was 25 per cent., while among 302 fit soldiers, and those suffering from injury or gonorrhoea, the incidence was only 15·5 per cent. A further analysis of the former sub-group revealed the highest incidence to be among 46 patients suffering from respiratory diseases, in whom the incidence of sickling was 28·3 per cent. No significant variation from the figure of 25 per cent. was found for any other group of diseases.

F. Murgatroyd.

English, R. B. **A Note on the Occurrence of the Sickle-Cell Trait in the Blood of a Bantu.** *South African Med. J.* 1943, Dec. 25, v. 17, No. 24, 389–90.

The author states that though the sickle-cell trait is confined almost entirely to negroes and half-whites, and has been found in certain white races, it has not hitherto been reported in the Bantu. He records a case in a young adult male Bantu of a tribe originating in Angola. The trait was not present in two persons alleged to be brother and sister of this man. *Charles Wilcocks.*

VENOMS AND ANTIVENENES.

Bovet, F. & Bovet, D. Application de la méthode de Warburg à l'étude de l'action estérasique du venin de cobra. [**Warburg's Method for studying the Action of Cobra Venom on Esters.**] *Ann. Inst. Pasteur.* 1943, Sept.–Oct., v. 69, No. 9–10, 309–12, 3 figs.

Delezenne and Fourneau have shown that cobra venom hydrolyses lecithin and sets free lysocithin, a haemolytic substance, by a sort of ferment action. The venom acts rapidly on yolk of egg, but very slowly on pure lecithins prepared from it. The former being a complicated reaction, the authors have studied the more simple hydrolytic activity of the venom on other glycerin esters or choline ; in the present contribution on acetylcholine. To this end they have used the manometric method of Warburg. They find, rather unexpectedly, that the rapidity of the reaction is, within wide limits at least, independent of the concentration of the acetylcholine. A graph shows that the hydrolysis is just as rapid at the beginning with a concentration of 1/250 as one of 1/2,500 ; there is no latent period. Another peculiar feature is the relative independence as regards temperature at which the reaction is carried out. The rate was the same at 20° as at 37°C.

Some authorities state that Ca ions favour the action of venoms on lecithin, but the authors found nothing to confirm this.

The question of inhibition of the diastatic effect of venoms is of much interest, but, say the authors, it has not been investigated. They have now shown that eserine has such an action, inhibition being almost total in a concentration as low as 1 in 2,000,000. Methylene blue has a similar effect but at a higher concentration, 1/1,000.

The authors conclude that the venom contains more than one esterase on the grounds that the action on choline esters takes place at concentrations one-hundredth that on egg-yolk or triacetin, and that eserine inhibits the action of the venom on acetylcholine without impeding diastatic hydrolysis of triacetin and lecithin.

H. Harold Scott.

DERMATOLOGY AND FUNGOUS DISEASES.

MERRILL, E. D. **Dermatitis caused by various Representatives of the Anacardiaceae in Tropical Countries.** *J. Amer. Med. Ass.* 1944, Jan. 22, v. 124, No. 4, 222–4.

This is an interesting sequel to the article on "Dhobie Mark Dermatitis" previously abstracted [see this *Bulletin*, 1944, v. 41, 230, 231]. Anacardiaceae are widely distributed and it is a peculiarity of them that, though they are contact poisons, they produce fruits which are sought after and may be eaten with impunity—many mangoes, for instance. Only certain species of Mangifera, Senecarpus and Anacardium, members of the Anacardiaceae, are poisonous. The use of the sap for making lacquers is due to the milky product becoming brown or black on exposure to the air. This sap is present in all parts of the plant or tree and is not always irritating on contact, but develops this property later, and highly allergic persons may show a dermatitis on coming into contact with old furniture lacquered with it. Some persons also are known to develop a rash from eating mangoes; others develop dermatitis from coming into contact with the fresh leaves or after taking shelter under the trees in a shower, but generally it is the sap itself which is responsible.

The remainder of the paper refers to plants other than those belonging to the Anacardiaceae which may set up dermatitis, such as the Manchineel apple, and the stinging hairs of Jatropha and of Macuna.

H. Harold Scott.

DAVIS, E. L. **Mycotic Ear Infections at an Advanced Allied Base.** *Med. J. Australia.* 1943, Nov. 27, v. 2, No. 22, 437–8.

Twenty-two patients with mycotic or fungous infection of the external auditory canal were seen at an advanced allied base in the tropics during June and July 1943. Of these ten showed coexistent fungous infection of the glabrous skin on other parts of the body. It was possible to submit material for pathological investigation on only 16 of the cases, but the specimens from 11 of these revealed the presence of mycelium and spores; the material consisted of the waxy detritus, and skin flakes syringed from the external meati. About half of the specimens were greenish in tint owing to the presence of *Ps. pyocyanea*. The first stage of the disease is not often seen at clinics for there is then but soreness and tenderness on contact, with pain during chewing. Local examination at this stage reveals no obvious changes; but the external canal becomes red and inflamed during the next phase, whilst the canal is coated with a soft, moist, sebaceous-like detritus. In the third stage the walls become swollen so that the canal may be obliterated. The pain tends to be worse at night, and there is moderate pyrexia. In treatment a preliminary ear toilet was carried out; the ear was syringed, and swabbed with spirit. Glycerin and ichthyol (10 per cent.) tampons were then inserted. This routine was carried out for three or four days, by the end of which the acute stage had subsided. Subsequently the canals were daily swabbed with spirit as before, then painted with Castellani's carbol-fuchsin. Healing occurred after another four or five days. *Sydney Thomson.*

EARNSHAW, H. **A Method of Treatment of "Tropical Ear."** *Med. J. Australia.* 1943, Nov. 27, v. 2, No. 22, 438–9.

Attention is drawn to the various synonyms, "Singapore ear," "Panama ear," "surfer's ear," "hot weather ear," "otitis externa diffusa" and "desquamative external otitis." The treatment here described has been successfully used in nearly 200 cases and the average length of time required to effect a cure was twelve days. Most patients first present themselves when there is oedema of the meatus. The canal is at once packed really tightly and under direct vision with half-inch ribbon gauze. This is excruciatingly painful and may require light ethyl chloride anaesthesia, although most cases can be tackled if one-third of a grain of morphine be injected hypodermically one hour before the operation. The author insists that it is the pressure which is important and that ichthyol and glycerine are no more efficient than other medicaments. The formula, here recommended for use on the packing and as "drops," is a 5 per cent. suspension of mercuric ammonium chloride in liquid paraffin. The packing is left in place for forty-eight hours, the gauze being moistened twice a day with the above "drops." When there is much detritus, the canal must be cleansed as efficiently as possible, before proceeding with the subsequent routine treatment. This cleansing can be effected by syringing with a sodium bicarbonate solution, immediately followed by spirit so that the canal is dried. Thereafter, the "drops" are used three times a day, care being taken that they reach the tympanic membrane. No packs or plugs of any kind are inserted at this stage. Excoriations may be treated with the following ointment :—

Hydrarg. Ammon ...	24 grains
Zinc. Oxid.	1 drachm
Amyli	1 „
Paraff. Liq.	1 „
Adip. lan. hydros. ...	1 ounce

Most of the pain and much of the discharge disappear two days after the "drops" and ointment have been started. *Sydney Thomson.*

TROPICAL OPHTHALMOLOGY.

A REVIEW OF RECENT ARTICLES. XLIII.*

Trachoma.—GURD[1] prefaces an account of the features of trachoma as it occurs in the Maltese Islands with a useful and comprehensive review of the disease in general. His observations are based mainly upon the examination of Maltese recruits for the Services and 1,600 of these were seen. Five per cent. of them—dock-yard labourers and conscripts—showed signs of the disease : a number of those affected, however, were free from subjective symptoms and were quite unaware that they had any eye trouble. The author states that "The disease is not taken

* For the 42nd of this Series see Vol. 40, pp. 941–943.

[1]GURD, D. P. An Investigation into the Incidence of Trachoma in the Maltese Islands, its Early Diagnosis and Mode of Spread with special application to the Armed Forces. *J. Roy. Nav. Med. Serv.* 1943, July & Oct., v. 29, Nos. 3 & 4, 171–82 ; 237–39.

very seriously by the people themselves. It is for the most part very mild in character and gives rise to few distressing symptoms except when infection by secondary organisms supervenes." With regard to secondary infections the *Staphylococcus—albus or aureus*—appears to be the most common and diplobacillary infection to be the next most important. Early diagnosis is based upon the presence of tiny, greyish, round follicles in the tarsal conjunctiva of the upper lid, especially at the upper margin of the tarsus; these form round, pale eminences with conjunctival vessels running round their bases. Tiny petechial spots arranged in small plume-like clumps in a somewhat oedematous conjunctival membrane may also be seen. Corneal vascularization by invasion of the limbic vessels is revealed by the slit-lamp, and this constitutes an essential element in the diagnosis of the disease. It must be borne in mind that the limbal vessels may become more evident in conjunctival irritation from any cause. In trachoma, however, the vascularization is irregular, the extension of the terminal loops is peculiar, and foci of corneal infiltration are present.

Except during January and February there is little or no rainfall in Malta, and sunshine, glare and dust-laden winds are prevalent. A limited water supply is another factor predisposing to conjunctival inflammation. No case of entropion with trichiasis was observed amongst the recruits examined. Although this complication is common in Malta, it is only found in middle-aged or elderly persons of the poorer classes and is stated to be invariably associated with dental sepsis. Trachoma in Malta shows a very marked class incidence and affects only the lower strata of society.

Thorough application of a copper sulphate pencil proved satisfactory in the treatment of the more advanced cases of the disease. Oral administration of sulphonamides was found to have no influence on the trachoma but was beneficial in regard to secondary infections. The local application of 5 per cent. prontosil ointment is stated to have given good results when the cornea was affected.

An article in the *Royal Naval Medical Bulletin*[2] also deals with this subject and makes the same points. Stress is laid upon the importance of early diagnosis by use of the slit lamp and by examination of scrapings from the conjunctiva. Many Maltese serve as officers' stewards, and there is a danger that they may spread the infection should they suffer from the disease.

Stylianakis[3] reports favourably on the treatment of trachoma by prontosil. He states that the drug has proved its value and that its superiority over older methods of treatment with silver nitrate and copper sulphate is established. It has the advantages of being painless and capable of use in home treatment, and its use involves no injury to the lids by manipulation. In the later stages of the disease, when corneal complications are met with, he advises that the drug should be given by intramuscular injection supplemented by oral administration of 3–6 tablets. A lotion of 5 per cent. prontosil has been found effective.

Keratomalacia.—The part played by vitamin A deficiency in the causation of eye disease and blindness in Bengal has been the subject

[2] Roy. Nav. Med. Bull. 1943, No. 4, 6–13. Trachoma in Malta.

[3] Stylianakis, V. G. Im Antitrachom-Ambulatorium des Hygienezentrums von Canea angestellte Beobachtungen ueber die Trachom-Chemotherapie mit Prontosil. *Deut. Tropenmed. Ztschr.* 1943, Apr. 1, v. 47, No. 7, 161–9.

of a clinical investigation by KIRWAN, SEN and BOSE.[4] Night blindness, xerophthalmia and keratomalacia constitute the signs of a faulty nutrition. Night blindness, of course, is not in every case due to vitamin deficiency, but may be caused by various local morbid conditions. Glare, by its action on the visual purple, is a factor in the causation of nutritional night blindness; the regeneration of the purple, exhausted by exposure to strong light, is probably delayed or hindered when the diet is deficient in vitamin A. Some observers consider that conjunctival pigmentation is an early and characteristic sign of vitamin deficiency, whilst others are of opinion that this pigmentation, even when associated with Bitot's spots, is not necessarily a sign of such deficiency. Xerophthalmia is a degenerative condition characterized by dryness of the conjunctiva due to changes in the epithelium which impair secretory activity, and these changes respond to treatment with cod liver oil. Xerophthalmia and keratomalacia can be produced in animals by feeding them on a diet deficient in vitamin A. Clinically, a loss of conjunctival lustre can be observed, most marked on the temporal side, and a wrinkling of the bulbar conjunctiva occurs when the eyeball is rotated. Small, white, triangular spots appear on the temporal side of the limbus in the portion of the bulbar conjunctiva exposed by the palpebral aperture. These spots become covered by foam-like products of Meibomian secretion (Bitot's spots). Keratomalacia is described as an advanced stage of xerophthalmia. Impairment of corneal sensation and lustre occurs, infiltrations form and ulceration follows. The authors examined 200 patients complaining of night blindness. Fifty-one of these had retinal or optic nerve disease (23·5 per cent.). Of 106 night-blind patients, whose fundi appeared normal, 15 gave normal readings on examination with the biophotometer. In contrast 40 per cent. of controls, who made no complaint of night blindness and were free from any sign of diet deficiency, showed an impairment of dark adaptation. The incidence of night blindness in males was higher than in females; this can be explained by the greater liability of the former to be exposed to glare. Of 398 persons, in whom conjunctival changes were apparent——pigmentation, xerosis, or Bitot' spots, either alone or in combination——59·3 per cent. were normal as regards dark adaptation; but 83·5 per cent. of those with night blindness, and 84·2 per cent. of those with keratomalacia, showed one or more of these changes. Some loss of sensation, and slight loss of corneal lustre though the corneal epithelium was intact [an important point], were the earliest signs noted of involvement of the cornea. As the disease advances, areas of infiltration or degeneration appear in the deeper layers of the cornea, whilst the epithelium remains intact. Later the cornea begins to disintegrate rapidly. Treatment of slight cases with cod liver oil or shark liver oil by the mouth was satisfactory in the absence of gastro-intestinal or liver disorders. Shark liver oil was found to contain four times as much vitamin A and twice as much vitamin D as cod liver oil. Severe cases were treated by parenteral administration of vitamin A preparations. The authors conclude that conjunctival pigmentation, either alone or in combination with xerosis or Bitot's spots, is not necessarily a sign of vitamin A deficiency.

[4] KIRWAN, E. O'G., SEN, K. & BOSE, N. Nutrition and its bearing on Preventable Blindness and Eye Diseases in Bengal. *Indian J. Med. Res.* 1943, May, v. 31, No. 1, 49–62. [55 refs.]

Diabetic Retinitis.—BOCK[5] has studied diabetic retinitis seen in Chinese patients. He found that 26 per cent. of 183 Chinese diabetics suffered from the disease. Diabetes in the Chinese seems usually to be of a fairly mild type and to be less often complicated by hypertension and arteriosclerosis than in western peoples. Nearly half of those suffering from diabetic retinitis were free from signs of hypertension, retinal arteriosclerosis or renal disease. The age group of diabetics showing the highest incidence of retinitis was that between 50 and 60, and the average duration of the diabetes before the onset of ocular complications was about seven years. No striking difference as regards hypertension, arteriosclerosis, acetone bodies, cholesterol and renal function was noted between those patients with retinitis and those without, but a higher blood sugar content was observed in the former group. An increased blood sugar content persisting over a long period may damage the capillaries and thus indirectly cause the ocular trouble. Retinitis is seldom seen in youthful diabetics though their blood sugar content is high. But this may be explained by the fact that young diabetics either succumb to the disease before retinitis can develop or their blood sugar is reduced by insulin treatment. The blood vessels of young persons, too, are likely to be more resistant to damage than those of older people. *H. Kirkpatrick.*

VENABLES, H. P. & POLLOCK, F. J. **Rickettsias in Ophthalmology.** *Arch. Ophthalm.* 1943, Sept., v. 30, No. 3, 362–70, 4 figs.

MISCELLANEOUS.

NEHAUL, B. B. G. **Report on the Physical Development and Health of a Sample of School Children in the Island of Leguan, British Guiana, 1941.** *British Guiana Med. Ann.* 1943, 95–113.

There is a population in the Island of some 3,500 persons, the majority of whom are East Indians. This is a preliminary report on the examination for physical defects of 138 of the children. A summary is given of previous inspections of children in British Guiana. In 1917 F. G. ROSE examined 706 school children in four Georgetown schools. The chief finding was the extraordinary low standard of nutrition associated with anaemia and a high frequency of infection with intestinal parasites (*Ascaris* 60 per cent., *Enterobius*, *Trichuris* and hookworm 2 per cent.). There was very little evidence of malarial infection. Enlarged tonsils and adenoids were rarely found. The condition of the teeth was reported as excellent. A large number of children were infected with scabies and tinea. There was no evidence of pulmonary tuberculosis. In 1920 Rose inspected 10,006 children between the age of 3 and 16 in the country schools of the East Coast, Demerara County. The general findings were similar to those found among the children examined in the Georgetown schools.

In the Island of Leguan the housing and sanitary conditions are of very low standard, the subsoil water rises to near the surface and

[5] BOCK, R. H. Diabetic Retinosis in the Chinese. *Arch. Ophthalm.* 1943, June, v. 29, No. 6, 919–23. [19 refs.]

floods are frequent, the warm muddy soil being ideal for hatching hookworm eggs. Almost everyone goes barefoot. The main findings of the examination were the following: approximately two-thirds of the children had dental caries, either of temporary or permanent teeth or of both. SNEATH in 1920 reported dental caries in one-quarter of the boys of all races in Queen's College, but these boys came from more affluent homes and were better fed than the children in the country schools. Enlarged tonsils and adenoids among Leguan children reach the high figure of 64 per cent., whereas Rose found only 2·6 per cent. among the children of Demerara County. Variations in standard may account for some of these differences. Every child examined had enlarged glands, either cervical, axillary or inguinal. Many showed enlargement in two or all three areas. In no case was tuberculosis considered the cause, whereas Rose reported tuberculous glands in 21·2 per cent. among the boys attending Queen's College. Two only of the Leguan children showed evident signs of filariasis but no blood film examinations were made. Rose reported 52·5 per cent. Four-fifths of the Leguan children had anaemia, four times the number reported by Dr. Rose. Hookworm, malaria and under-nourishment probably accounted for most of it. Sixteen per cent. of the children under the age of 16 had enlargement of the spleen; Rose found double the number from the country districts of Demerara. The percentage among East Indians was much higher than among blacks, though both races were similarly exposed to malaria. Lice were very commonly found among East Indian children but rarely among the blacks. Skin disease, including eczema, was rarely found. There was no evidence of disease due directly to vitamin deficiency. Defects of vision were very slight. Anthropometric measurements were made but will be presented later, the author confining himself to the comment that the physical development of the children is much better than is popularly believed.

Perhaps the chief value of this strictly limited inquiry, and the comparison of the findings with those of previous investigators, is to show the necessity for a more planned inquiry among both town and country children, having special regard to the different conditions which appear to be found even in adjacent geographical areas. If carried out by more than one medical officer, closest attention would need to be paid to the question of standards, and the extent and degree of defects found. Short of this, comparison among different groups of children may be, in regard to some findings, almost valueless.

Ralph H. Crowley.

PAVLOVSKY, E. **Parasitological Expeditions in the U.S.S.R.** *Voks Bulletin.* Moscow. 1943, No. 3–4, 29–32, 4 figs.

The English reader is here provided with an interesting general account of the exploration of the U.S.S.R. for parasites of man. The paper is authoritative, and produced by the man who has directed a very large part of what is here described, organizing and often leading expeditions to remote and very little known areas. The map which accompanies the article shows that expeditions from Moscow have repeatedly gone to the Russian Far East and to the group of republics lying between the Caspian and China. On these expeditions, experts of many types, medical men, parasitologists, entomologists, and so forth have all had their share, recording the distribution of the parasites and studying the biology in the field.

The authors give a brief and rather general account of a number of interesting, unusual conditions and infections, for instance tick borne relapsing fever, the encephalitis transmitted by ticks (*Ixodes*) in the Far East, and the relation of the gerbil (*Rhombomys*) to sandfly and oriental sore in the valley of the Murgab. No reference is made to malaria, presumably because the outline of its parasitology is familiar to most well informed people. *P. A. Buxton.*

ROYO MONTAÑÉS, M. Patologia infantil marroquí. [**Disease in Moroccan Infants.**] *Med. Colonial.* Madrid. 1943. Dec. 1, v. 2, No. 6, 407–25, 3 figs.

No figures are given in this article: the subject is considered in very general terms. For the first year of life the Mussulman child is kept very much secluded, shut up in the house, rarely allowed out, with the minimum of exposure to the sun's rays; he is fed wrongly, either the breast-feeding being supplemented by unsuitable articles of diet, or the lactation kept on long after the mother is able to furnish any nutriment of value. Rickets is in consequence very rife among them, and death from a complicating broncho-pneumonia. "Syphilis, conjoined with rickets, is decimating the infant population of Morocco."

H. Harold Scott.

LALINDE DEL RIO, E. Organización sanitaria en los territorios españoles del Golfo de Guinea. [**Health Organization in the Spanish Territories of the Gulf of Guinea.**] *Med. Colonial.* Madrid. 1943, Jan. 1, v. 1, No. 1, 53–9, 3 graphs.

The Spanish territories of the Gulf of Guinea include not only part of the mainland, but the islands of Fernando Po, Corisco, Elobey Grande, Elobey Chico and Annobon. The continental portion has an area of 26,000 sq. kilometres and the inhabitants number 985 Europeans and 130,685 indigens; Fernando Po is 2,971 sq. kilometres, with a population of 1,426 Europeans and 34,204 natives. The total area is just over 28,105 sq. kilometres; Europeans number 2,364 and the natives 166,871. These are the figures given but the year of census is not mentioned. Every native has to carry a medical passport. These passports are of two kinds: (1) White, for healthy individuals, (2) Green for those with trypanosomes. These are revised from time to time, by calling up the possessors, examining their blood and the glands of any with adenitis, withdrawing temporarily their passports. The results of the examinations are noted on the passport. Any previously free from infection, but now found positive, gives up his white passport and is given a "Certificate of treatment" ("Cartilla de tratamiento"). The treatment may be "ambulatory" or the patient may be placed in hospital. If undergoing ambulatory treatment he may not travel from one zone to another without the permission of the local Chief Medical Officer; he is kept under observation and only when cure is proved can he exchange his Certificate of Treatment for a white passport and again move freely about the country. It all sounds very simple but it obviously entails an enormous amount of work if carried out conscientiously. Discreet medical officers are available for consultation by all persons in their areas and are also responsible for vaccination against smallpox, for anti-malaria measures, venereal disease

work, child welfare, and must be on the lookout for lepers, suspects being interned in the leprosaria of Ebebiyin and Mikomesen.

H. Harold Scott.

Firmino Sant'anna, J. A selecção médica dos recrutas e auxiliares das forças indigenas nas Colónias Portuguesas. [**Standards for Recruits in the Portuguese Colonies.**] *An. Inst. Méd. Trop.* Lisbon. 1943, Dec., v. 1, No. 1, 145–86.

This is a lecture delivered at the Military School of Tropical Medicine. The subject matter is carefully assembled and though it contributes nothing new it is useful as a reminder to those engaged in examination of recruits in the tropics of certain standards to be observed. The author divides his lecture into five sections. In the first he deals with the racial and regional aspects, pointing out that certain districts are known to be less healthy than others and that more caution is needed when examining or assessing a recruit from the Delta area of the Zambezi Province, for example, than when dealing with one from the interior. He next considers the standards of height, weight and chest measurement, and passes on to the diseases which would render a recruit unacceptable. The more obvious are mentioned, such as filariasis, schistosomiasis, ankylostomiasis, yaws, granuloma venereum, lymphogranuloma inguinale; he even mentions malignant tumours, which are hardly debatable in excluding recruits from acceptance. Under "medical preparation of new recruits" the author speaks of vaccination against smallpox, enteric fever, cholera, etc., and the prompt treatment of venereal disease. In the final section on "Special Pathology of the Newly-recruited", general advice is given as to the best means of warding off or guarding against malaria, enteric fever, pneumonia, venereal disease, etc.—in short, suggestions for applying common sense.

H. Harold Scott.

Bharucha, D. R. **Report on Tropical Ulcers.** *Indian Med. Gaz.* 1943, Nov., v. 78, No. 11, 532–5.

In a period of six months 179 Indian soldiers were admitted to one hospital [presumably in India] with tropical ulcer. Almost all these men came from one particular area, but no correlation could be found between the incidence of ulcer and the rainfall or humidity of that area. All patients had been receiving standard army diet, known not to be deficient in any important factor. The men had been engaged in extensive and strenuous military exercises at the time of highest incidence, and 160 gave a history of some form of injury to, or inflammation of, the skin of the part, which had preceded the development of the ulcer.

Investigations were made. No significant bacteriological findings are reported, in spite of attempts at cultivation, and of routine examination of smears; only staphylococci and diphtheroid organisms were found frequently. Kahn and Wassermann examinations were positive in only 5 of 107 men tested. About 10 per cent. of the patients were passing hookworm eggs, but there was no appreciable effect of this infestation on the haemoglobin or the red cell count. Dysentery, malaria, anaemia and avitaminosis were not present in active form in this series of cases. On this evidence, therefore, the author is forced to the conclusion that the significant aetiological factor is slight

trauma, with neglect of the small wound, leading to septic infection. In most cases there was a considerable interval between the onset of the ulcer and admission to hospital.

Two forms of treatment were used. In the first the ulcers were dressed daily with 1 in 150 copper sulphate solution until the slough had gone, and then with 40 per cent. cod liver oil in vaseline, under occlusive elastoplast, changed every 5–7 days. With this treatment the average stay in hospital varied from 35 to 54 days, according to the size of the ulcer. The second (and more successful) treatment consisted of dressing the ulcers daily in the acute stage with a powder of equal parts of sulphonamide [not further specified] and iodoform, and, in the healing stage, with red lotion, the dressing being changed every 3–5 days. In this treatment occlusion dressings were not used because they irritated the skin and tended to produce daughter ulcers. Length of stay in hospital was reduced, under this treatment, to averages of 20–36 days. A most important feature of all treatment was rest to, and elevation of, the affected part, enforced, if necessary, by application of back splints with foot pieces to both legs. *Charles Wilcocks.*

ROMERO MOLINER, R. El factor vascular en la ulcera tropical y su tratamiento. [**The Vascular Factor in Tropical Ulcer; its Treatment.**] *Med. Colonial.* Madrid. 1943, Dec. 1, v. 2, No. 6, 401–6. [18 refs.]

Local deficiency of blood-supply may be due to obliteration of vessels or to vascular spasm. Tropical ulcer, according to the author, produces stimuli which irritate the sympathetic and maintain vasospasm. The beneficial effect of quinine in tropical ulcer is ascribed to "affection of the suprarenal cortex by chronic malaria which indirectly, *via* the adrenal deficiency, favours ulceration" [a far-fetched theory which the author supports by the results of treating gastric ulcer by cortical hormone]. BAUER has recorded good results with folliculin, and WAGNER with synthetic oestrogen locally.

For treatment of tropical ulcer the author massages the parts surrounding the lesion to obtain vasodilatation and to maintain it employs "anaesthetic elimination of the sympathetic" by local injection of 2 per cent. novocaine around the ulcer. The patient feels in a few minutes a sense of heat on the surface of the ulcer, intense for 4–5 hours and then passing off gradually. The following results are stated to occur: (1) Rapid subsidence of the oedema and pain. (2) Normal appearance of scar-tissue without peripheral thickening. (3) Favourable course without relapse. *H. Harold Scott.*

SERRAS SIMÕES, T. Aspectos clinicos de certas lesões supuradas dos membros; deduções profiláticas e terapêuticas, baseadas no emprêgo de injecções intra-arteriais de mercurocromo. [**Suppurative Lesions of the Limbs. Treatment by Intra-arterial Injections of Mercurochrome.**] *An. Inst. Med. Trop.* Lisbon. 1943, Dec., v. 1, No. 1, 127–43, 2 figs. on 1 pl. [26 refs.]

By "suppurative lesions" the author implies "ulcers"; at all events he deals with ulcerations only. He divides them into three groups: (1) From infected wounds, often from small injuries sustained

at work, or secondary to insect-bites. He includes in this group lesions due to scabies, to syphilis, yaws, and varicose ulcers [a strange medley to group together]. (2) Phagedaenic ulcers, associated with trauma, yaws, syphilis, leishmaniasis, mycoses, tuberculosis, and in diabetics, alcoholics and the debilitated. (3) Atonic ulcers, chronic, with little secretion and small granulations, without affecting the bones, associated with the common pyogenic organisms. [An unsatisfactory classification, because the groups overlap and are far from being distinctive]. The evolution of the ulcers varies naturally with "the virulence of the microbic flora and their toxins and the reaction on the part of the patient."

The author claims good results from intra-arterial injections of 5–10 cc. of 2·5 per cent. mercurochrome (in very severe lesions 5 per cent. strength is used), 3–5 injections at 3–5-day intervals, into the superficial femoral at the base of Scarpa's triangle for leg ulcers. If more than five injections are given there is a tendency to stomatitis. At the same time local applications of Dakin's solution or of potassium permanganate are made. In addition to the mercurochrome, in severe cases the author injects 2 per cent. biniodide of mercury, a drop at a time, in two or three places 2·5–3 cm. apart around the edge of the ulcer. In cases of deep ulceration to bone all three forms of treatment—mercurochrome injections, biniodide of mercury and permanganate of potassium or Dakin's solution—are combined and when the phagedaenic process is stopped the edges and base of the ulcer are removed till healthy tissue is reached. Similar resection of the edges may be needed for Group 3 cases. *H. Harold Scott.*

CHAUDHURI, R. N. **'Eosinophil Lung.'** *Indian Med. Gaz.* 1943, Dec., v. 78, No. 12, 575–7, 4 figs. (2 on pl.).

INDIAN MED. GAZ. 1943, Dec., v. 78, No. 12, 599–600. **Marked Eosinophilia with Lung Infiltration.**

Another, very typical, example of this condition which has been attracting much attention of late. The patient was a Mohammedan, 31 years of age, admitted to hospital with a history of fever for ten days, weakness and loss of weight, and a dry, troublesome cough. After an afrebrile period of six days his temperature again rose and the cough was worse. His blood contained 29,500 leucocytes per cmm., of which 22,272, or 75·5 per cent., were eosinophiles; the lungs showed by X-rays diffuse mottling suggestive of miliary tuberculosis, though the patient did not seem to be sufficiently ill to warrant this diagnosis; auscultation revealed a few rhonchi, especially at the right base behind. The usual causes of eosinophilia, such as asthma and helminthic infestation, could be excluded. No treatment, except sedatives for the cough, was given for a week during which the patient was kept under observation, and his fever and cough continued. He was then given a course of mapharside injections, 0·02 gm. for the first, and 0·04 gm. for four subsequent doses, at five-day intervals. His temperature became normal after the second injection, the cough subsided after the third and the mottling of the lungs cleared up. Weekly blood-counts revealed leucocytes 14,000, 13,500, 10,600, and 6,200, with eosinophile percentages of 69·5, 56·5, 27 and 16 respectively. In a fortnight he gained 10 lb. in weight. [See this *Bulletin*, 1941, v. 38, 538, 539; 1943, v. 40, 720, 721, 948; 1944, v. 41, 425.] *H. Harold Scott.*

FAWCETT, D. W. & GENS, J. P. **Magnesium Poisoning following an Enema of Epsom Salt Solution.** *J. Amer. Med. Ass.*, 1943, Dec. 18, v. 123, No. 16, 1028–9.

Poisoning by magnesium sulphate is of very rare occurrence ; in 18 cases collected from the literature the illness followed oral administration and no case following rectal injection appears hitherto to have been reported.

One of the two cases described in the present paper was in a boy, aged 2 years, who was given an enema of magnesium sulphate after digital manipulation for faecal impaction ; he had been operated on two months before for imperforate anus for which a colostomy had been done ten days after birth. The enema was returned with good results but almost immediately the child stopped breathing and became unconscious. Slight irregular abdominal breathing was resumed after artificial respiration, oxygen therapy and an injection of nikethamide, but the child died of respiratory failure a few hours afterwards.

The other patient was an Italian woman, aged 23 years, who was admitted with a ureteral calculus. She was given prostigmine methyl sulphate, followed in 15 minutes by a small enema of 4 fluid ounces containing approximately 1½ ounces of glycerine and 1 oz. of magnesium sulphate. This was retained for two minutes only, a considerable amount of fluid being passed ; two more large fluid motions were passed at intervals of 10 minutes, and immediately after the third, the patient complained of feeling hot all over and of being very thirsty. This was at about 6·30 a.m. and at 7·15 a.m. she became almost unconscious with shallow respiration, flaccid limbs and loss of all reflexes including the corneal reflex ; there was incontinence of faeces but not of urine. One gramme of calcium gluconate was given intravenously and this was followed by improvement in the respiration, and some movement of the head was observed. The calcium injection was repeated 10 minutes later, and after another 10 minutes the patient recovered consciousness and asked for water. The corneal reflex did not reappear until 2–3 hours later. It was found that the stone had been passed and the patient was discharged from hospital three days afterwards. Analysis of her blood, taken at the time of the first calcium injection (9 a.m.), showed 28·8 mgm. of magnesium in 100 cc. [normal 4 mgm].

The authors think that complaints of feeling hot all over and very thirsty should be taken as premonitory signs of impending poisoning in these rare cases and that it can be prevented by the immediate intravenous injection of calcium. *J. F. Corson.*

FOX, H. **Yaws, Cutaneous Leishmaniasis and Pinta.** *J. Amer. Med. Ass.* 1943, Oct. 23, v. 123, No. 8, 459–62.

This is a general account of the three diseases, in which no new work is reported. It has been written as an aid to medical officers who may be called upon to treat native populations, but a warning is given that although it is not probable that many American troops will contract yaws and pinta, they may acquire cutaneous leishmaniasis.

Charles Wilcocks.

DORMER, B. A., FRIEDLANDER, J. & WILES, F. J. **A Note on Jigger Flea (*Tunga penetrans*) Infestation in Man.** *South African Med. J.* 1943, Dec. 25, v. 17, No. 24, 382, 2 figs.

The authors state that, to judge from the literature, no instance of human infestation with *Tunga penetrans* has been reported from South Africa. They encountered a case in southern Natal, from which characteristic gravid *T. penetrans* were recovered. A questionary to District Surgeons in Natal showed that none had encountered the parasite, but enquiries among the natives made it clear that infestation is not uncommon in the coastal areas. *Charles Wilcocks.*

APPELMANS, M. & GATHY, J. Kératite par poils de chenille "Porthesia Similis." [**Keratitis caused by the Hairs of the Caterpillar *Porthesia similis*.**] *Ann. Soc. Belge de Méd. Trop.* 1943, Mar. 31, v. 23, No. 1, 3–11.

In this article, from the ophthalmological clinic of the University of Louvain, Belgium, the authors record in some detail a case of inflammation of the eye due to the poisonous hairs of a caterpillar of the species *Porthesia similis*.

When disturbed the caterpillar secretes an irritant fluid from glands on the dorsum of its posterior segments; the secretion dries on the adjacent hairs and can cause intense itching of the skin and inflammation of the eye. The latter develops in two phases; at first there is a reaction to the irritant secretion with swelling of the eyelids, conjunctivitis and superficial keratitis, the cornea showing superficial spots and vesicles. This phase is characterized by pain, lachrymation, photophobia and diminished vision. The effects gradually subside and the second phase appears as a chronic reaction to the hairs as foreign bodies; they cause little irritation but opaque nodular granulomata are formed which are seen, through the microscope, to lie in the middle and deeper layers of the cornea.

The case recorded was that of a seven-year-old girl into whose eye a caterpillar was thrown and caused the signs and symptoms described above. Innumerable caterpillar hairs were imbedded in the parenchyma of the cornea. During the following two weeks the inflammatory condition gradually subsided. After two months the cornea became clearer but oblique illumination showed little spots of infiltration like superficial punctate keratitis; ulceration had caused shedding off of the superficial hairs but others remained in the deeper layers of the cornea. These spots became more numerous and some peripheral vesicles appeared; pericorneal injection persisted. The anterior chamber and iris were unaffected.

Four months after the accident the cornea showed very fine opaque stippling in the middle and deeper layers, corresponding with the hairs; the pericorneal injection had disappeared. After another six weeks flaky deep opacities were still present but the hairs were fewer and hardly visible. Vision of the eye remained at one-half of normal.
J. F. Corson.

ALLISON, R. S. & CRITCHLEY, M. **Observations on Thirst.** *J. Roy. Nav. Med. Serv.* 1943, Oct., v. 29, No. 4, 258–66, 1 fig.

Three healthy sailors were submitted to a test of water deprivation during a period of hot weather [presumably in Britain]. On the first

day full diet and 5 pints of fluid were allowed to each man, on the following 3 days lifeboat rations were given (1 oz. pemmican, 3 biscuits, 1 oz. dried milk tablets and 1 oz. chocolate). One man took no fluid during the experiment, the second man was allowed 4 ounces, and the third 8 ounces, of water each 24 hours. On the fifth and sixth days full rations and 5 pints of fluid were given to each man. The men were kept in bed under constant observation, but were allowed to smoke, talk and write. Urine and blood analyses were made each morning, and twice each day the men were examined physically, special attention being paid to pulse rate, respiration rate, temperature, blood pressure and exercise tolerance by a standard test. A record of body weight was kept.

All three lost weight (7–12 lb.) which, however, was rapidly regained after the test was completed. There was little change in resting pulse rate, respiration rate, body temperature and blood pressure, but the standing pulse rate was increased and tachycardia was much increased in the exercise tolerance test. This response resembled that seen in the effort syndrome.

The blood sugar and blood urea levels were not significantly raised. The volume of urine passed diminished greatly, and the specific gravity rose, the percentage of urea reaching 4·17 in one case. Total daily output of urinary chloride fell as follows: Subject A, from 11·53 to 2·18 gm.; B, 7·27 to 1·2; C, 6·36 to 1·4. [Subject A took no fluid, B took 4 oz. daily, C took 8 oz. daily.] There was slight increase in blood chloride.

All three showed evidence of haemoconcentration as increase of haemoglobin percentage and raised red cell count, but the increases were not great.

The results of psychological investigation did not reveal any material change.

Little objective difference was found between the man who took no water and the other two who received small amounts.

Various palliative methods were tried, in two other men suffering from diabetes insipidus, with the object of relieving the sensation of thirst; all failed. Gargling, chewing gum, the rectal instillation of fresh or sea water, and other measures were useless. In the three subjects deprived of water, thirst was not quenched even by repeated drinks, at the end of the experiment, until body weight had been stabilized at the original level. *Charles Wilcocks.*

ROBINSON, S., TURRELL, E. S., BELDING, H. S. & HORVATH, S. M. **Rapid Acclimatization to Work in Hot Climates.** *Amer. J. Physiol.* 1943, Nov. 1, v. 140, No. 2, 168–76, 2 figs. [20 refs.] [Summary appears also in *Bulletin of Hygiene.*]

With acclimatization to heat man's ability to do prolonged physical work increases. In the study described in this paper the authors set out to measure this improvement in heat tolerance, and to follow its time relations.

The experiments were carried out in Boston in the cool weather (February and March), in an artificially heated room where the temperature was maintained at 104°F. and the humidity at 23 per cent. The work done by the subjects consisted in walking on a treadmill at 3½ miles per hour. Four of the five subjects walked on a gradient of 5·6 per cent., and the other on a gradient of 4·0 per cent. The duration of the walking period throughout all the main series of experiments

was determined separately for each subject; it was the time required to exhaust him at the beginning of the investigation. The times varied between 1 and 1½ hours. These standard hot room walks were continued until the men had trained for from 10 to 23 days. Three of the subjects spent an additional 3 to 4 hours a day in the hot room making observations on other subjects. All the subjects were laboratory workers accustomed to walking on the treadmill, but none had been exposed to heat since the preceding summer. All were in good physical condition. Standard clothing was worn during the experiments: it consisted of U.S. Army summer cotton trousers, shirt, tie, woollen socks and service shoes. Physiological determinations included pulse rates, rectal temperatures, skin temperatures (chest, back, thigh and upper arm), rate of water loss—found by weighing—and oxygen intake.

The subjects walking on the steeper grade approached heat exhaustion in the early experiments, with high skin temperatures, rectal temperatures of 103° to 104°F., and heart rates averaging 178 beats per minute during the last 20 minutes of work. Repetitions of the constant task increased the comfort and ease with which the work was performed, and about 80 per cent. of the improvement noted occurred in the first seven days of exposure. The heart rates of the men during the latter part of the walks declined from an average of 178 in the beginning to 155 on the seventh day; and during the same period the average skin temperatures at the end of the work experiments fell from 98·4 to 96·5°F., while the rectal temperatures declined from 103·4° to 101·7°F. This improvement in temperature regulation was accompanied by an increase in the rate of sweating in one man, and by decreases in the metabolic rate during work in the others. The further slow improvement in temperature regulation after the seventh day was not accompanied by continued lowering of the metabolic rate nor by increase of sweating during the experiments. But the ability to sweat in harder work than the standard experiments did increase.

After 23 days of exposure, two subjects repeated the standard walk with the room temperature reduced to 72°F., and in these walks they reached heat balance with their rectal temperatures and metabolic rates the same as they were in the hot room at the end of acclimatization.

It is clear from the data adduced in the paper that physically fit persons can be expected to work effectively within a few days after they start work in a hot climate. By a few relatively short daily exposures to work in artificially heated rooms they can be prepared for working immediately after they arrive in a hot climate. This process of acclimatization is no substitute for the training necessary to produce good physical condition, which is also essential before fit men can work effectively in the heat. *T. Bedford.*

BOOK REVIEWS.

CRAIG, Charles Franklin [M.D., M.A. (Hon.), F.A.C.S., F.A.C.P., Colonel, U.S. Army (Retired), D.S.M., etc.] & FAUST, Ernest Carroll [M.A., Ph.D., etc.]. **Clinical Parasitology.** Third Edition, thoroughly revised. 767 pp. With 284 engravings & 4 coloured plates. 1943. London: Henry Kimpton, 26 Bloomsbury Way, W.C.1. [45s.]

The past success of this book is evident in the appearance of yet a third edition within three years of its predecessor. This edition comes

at a particularly apposite time, when the war activity is extending further over tropical and subtropical areas. Many who have previously regarded the human parasitic diseases as remote and intangible entities are now encountering them on a large scale; to these Craig and Faust will afford a valuable source of information. The third edition is slightly larger than the second; while the general scope and arrangement are the same, there is some elaboration, more especially in the fields of epidemiology and therapeutics. There are many new figures in the text, four coloured plates of the malaria parasites have been introduced, and two clinical tables, with cross references to pages in the text, have been inserted at the end of the work. These tables show the salient diagnostic points and the treatment, respectively, of parasitic and arthropod-conveyed infections of man. The quality of the coloured plates is somewhat disappointing in this clearly printed and well-bound volume. Within the limitations of space necessarily imposed by the incorporation of so much matter it is inevitable that statement is at times sweeping. This may lead to erroneous impressions; for example, on reading the article on the treatment of malaria one is left to wonder why quinine is used at all when atabrine (mepacrine) appears so superior on every count but that, possibly, of toxicity. Again, from the account of the treatment of amoebic dysentery it appears that the infection is very easily eradicated; such statements as that chiniofon by the mouth "is usually curative in 'asymptomatic carriers'," and "Rarely resistant infections are encountered," in which case other drugs may have to be used, will not meet with universal acceptance. A serious omission in the articles on the treatment of the leishmaniases and of the African trypanosomiases is lack of reference to the diamidine series of drugs which have proved so valuable in the Mediterranean type of kala-azar, where the antimonials are frequently ineffective. But these are minor matters in comparison with the successful achievement of the authors' main purpose, *viz.*, to give a concise and lucid account of the parasites which infest man and of the harmful effects of their presence.

A. R. D. Adams.

MENDES DE CASTRO, B., GIORGI, Dante & KIEFFER, Julio C. **Contribuição ao estudo da Pelagra.** [Contributions to the Study of Pellagra.] 181 pp. With 18 figs., 8 graphs & 30 charts. 1941. S. Paulo. [Bibliography.]

Presented in book form, the first hundred pages are devoted to a consideration of history, geographical distribution, aetiology, symptomatology, etc.; then follow 75 pages given up to reports of 30 cases studied in São Paulo Hospital between March 1938 and February 1940.

The volume will doubtless serve the purpose for which it was written and be read in Brazil, but it contains nothing new and, having been published in 1941, is already somewhat out of date.

Unfortunately too there are many misspellings of names and many omissions, geographical distribution, for example, being most inadequately dealt with.

H. S. Stannus.

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(508) Wt. P9/279 6/44 S.E.R. Ltd. Gp. 432.

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